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Living with paediatric chronic pain: a study of treatment outcomes and processes

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Appendices

Word count: 15,616

Abstract

This thesis investigated treatment outcomes and processes in young people with chronic pain. The first chapter describes a systematic review, which examined the effectiveness of acceptance and mindfulness-based interventions in improving pain-related outcomes in young people. Secondary aims were to review changes in proposed treatment processes following the interventions, and to compare the effectiveness of these interventions to control conditions. Although there was evidence to suggest that these treatments may improve outcomes, particularly levels of daily functioning, further research is needed to adequately assess the utility of acceptance and mindfulness-based approaches with paediatric chronic pain populations.

The second chapter details a cross-sectional study of contextual and cognitive processes in adolescents with chronic pain. Specifically, the study tested the mediating effects of acceptance, catastrophising and kinesiophobia in the relationship between pain intensity and indicators of adjustment. Both acceptance and kinesiophobia mediated the effects of pain intensity on disability and quality of life, while catastrophising mediated the effect of pain intensity on levels of anxiety and depression. The results demonstrated that both contextual and cognitive factors are important determinants of young people's well-being. Future research would benefit from gaining a greater understanding of how these processes interact with each other to affect pain-related outcomes.

Lay Summary

This thesis is composed of two chapters which explore how psychological interventions and mechanisms affect the well-being of young people who have chronic pain.

The first chapter examined how effective a group of psychological therapies called *acceptance and mindfulness-based interventions* were in improving the pain levels, daily functioning, mood and quality of life of young people who have chronic pain. It also looked at whether these treatments impacted on the psychological mechanisms targeted in treatment. A final aim of this chapter was to see whether these treatments were more effective than other treatments or no treatment at all. Most studies found that these treatments improved young people's ability to perform daily tasks. The studies differed more in whether they found these treatments useful in improving pain intensity, mood and quality of life; and whether they were better than other treatments or no treatment. The review found that more research with bigger groups of participants is needed to determine the effectiveness of these interventions.

The second chapter investigated whether adolescents' thoughts and fears about their pain, and the degree to which they were willing to accept their pain, influences their well-being. The study found that both accepting their pain, and having fears about doing physical activity and being injured, influenced how adolescents rated their quality of life and their ability to perform daily tasks. In contrast, having catastrophic thoughts about their pain affected their levels of anxiety and depression. The study concluded that these factors should be considered when providing psychological therapy to adolescents with chronic pain.

The effectiveness of acceptance and mindfulness-based interventions in improving outcomes for young people with chronic pain: a systematic review

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Prepared in line with the guidelines for Behaviour Research & Therapy (see Appendix A).

Highlights

- These interventions may be effective in improving pain-related outcomes and processes.
- The efficacy of these treatments over control conditions is unclear
- More high quality evidence is needed in the field.

Abstract

Background: Acceptance and mindfulness-based interventions have emerged as promising treatments for chronic pain. To date most reviews have focused on adults. This review aimed to evaluate the effectiveness of these interventions in improving outcomes for young people with chronic pain. Secondary aims were to examine changes in treatment processes, and to compare these approaches to control conditions.

Method: A literature search for intervention studies examining within-group effects of acceptance and mindfulness-based treatments with paediatric chronic pain populations was conducted. A range of electronic databases were searched, the reference lists of eligible studies were examined, and a number of experts in the field were contacted in order to find published and unpublished studies.

Results: Nine studies were suitable for inclusion. Results indicated that these interventions may be effective in improving the well-being of adolescents with chronic pain, particularly in the domain of daily functioning. There was also evidence to suggest that these approaches may increase psychological flexibility.

Conclusion: While acceptance and mindfulness-based interventions demonstrated some promising results, limitations in the evidence-base preclude strong conclusions. As such, further research, using more rigorous methods, is warranted.

Keywords:

Acceptance, Mindfulness, Chronic Pain, Child, Adolescent

Introduction

A significant proportion of young people experience chronic pain, characterised by persistent or recurrent pain lasting three months or longer (King et al., 2011). Although many of these young people do not report extensive pain-related distress or disability, a subset experience substantial interference in daily functioning and quality of life (Huguet & Miró, 2008; Palermo, 2000), and also co-morbid mental health difficulties, which may persist into adulthood (Noel, Groenewald, Beals-Erickson, Gebert, & Palermo, 2016).

The psychological treatment of paediatric chronic pain has been dominated by behavioural interventions, such as relaxation training and biofeedback; and cognitive behavioural therapy (CBT), which combines behavioural techniques with cognitive strategies, such as guided imagery and cognitive restructuring. This is illustrated in recent reviews examining the effectiveness of psychological therapies for paediatric chronic pain, in which such approaches represented the vast majority of treatments examined (Eccleston et al., 2014; Fisher et al., 2014). While these reviews demonstrated the ability of such approaches to reduce young people's pain compared to control conditions, the evidence was less convincing for other outcomes, with only small effects observed for disability, and largely no effect observed for mood. Pielech, Vowles & Wicksell (2017) argue that the emphasis on pain reduction within CBT may inadvertently increase a person's functional disability through avoidance of pain-related activities, a perspective which may account for some of these findings.

A new generation of cognitive-behavioural therapies has emerged in recent decades, and have become increasingly popular treatments for chronic pain. Such approaches are commonly referred to as *third-wave* treatments (Hayes, 2004), *acceptance and mindfulness-based* interventions (Hayes, Follette, & Linehan, 2004), or *contextual cognitive behaviour therapy* (CCBT; Hayes, Villatte, Levin, & Hildebrandt, 2011). Unlike treatments which focus on controlling and reducing pain and distress, these interventions aim to help clients become aware of and accept their pain as part of life. They are interested in the context and function of psychological events rather than their form or validity (Hayes et al., 2011). As such, an emphasis is placed on

changing one's response to symptoms instead of changing the symptoms themselves (McCracken & Volwes, 2014).

Prominent acceptance and mindfulness approaches used within chronic pain include mindfulness-based stress reduction (MBSR; Kabat-Zinn, 1982, 1990), mindfulness-based cognitive therapy (MBCT; Segal, Williams, & Teasdale, 2002), and acceptance and commitment therapy (ACT; Hayes, Strosahl, & Wilson, 1999). These approaches aim to reframe emotional reactions associated with pain, and enhance resilience by fostering an attitude of non-judgemental acceptance towards thoughts, emotions and sensations (Baer, 2003). Such a stance helps clients to detach from beliefs and other internal experiences that may be limiting their life. Values clarification and committed action are additional components particularly within ACT. Through increased awareness and openness, clients are supported to reduce control strategies and increase their engagement in meaningful pursuits in the presence of pain (McCracken & Vowles, 2014). This is particularly relevant for young people who disengage in activities due to their pain, and in doing so increase their disability and distress (Pielech, Vowles, & Wicksell, 2017).

Researchers are increasingly investigating the effects of third-wave interventions, and have demonstrated some promising findings within adult chronic pain populations. For example, a recent meta-analysis of acceptance and mindfulness-based interventions noted small to moderate improvements in pain intensity, disability, quality of life, depression and anxiety following treatment (Veehof, Trompetter, Bohlmeijer, & Schreurs, 2016). A systematic review of ACT for adults with chronic pain also reported significant effects on physical functioning, anxiety and depression (Hann & McCracken, 2014). Both reviews, however, noted that the majority of control conditions were inactive, and consisted of treat-as-usual and waitlist groups. When acceptance and mindfulness-based approaches were compared to active treatments, Veehof et al. (2016) reported that CBT may be superior to third wave treatments, while the latter may be superior to MDT/relaxation interventions. However, none of these differences were significant in the pooled analysis (Veehof et al., 2016). Low quality evidence has also been highlighted as an issue within the field. Indeed, Veehof et al. (2016) noted that, despite the rapidly increasing evidence-base, the quality of studies had not improved since their previous review in 2011.

The authors of another recent meta-analysis also reported that no concrete conclusions regarding the efficacy of mindfulness meditation for pain-related outcomes could be drawn due to limitations in the methodological quality of the evidence (Hilton et al., 2017).

In contrast to the adult literature, researchers have only recently begun to examine third-wave interventions with young people with chronic pain. For example, a systematic review published in 2013, which examined mindfulness interventions in adolescent samples, identified just two studies involving chronic pain, both of which used ACT (Montegomery, Kim, Springer, & Learman, 2013). Results were mixed, such that large effects were observed in a small within-group study (Wicksell, Melin, & Olsson, 2007), while non-significant effects were reported in a follow-up RCT (Wicksell, Melin, Lekander, & Olsson, 2009). However, this review averaged scores across a number of mental health outcome measures in order to calculate effect sizes for a composite "psychological well-being" score, thus reducing the validity of their findings.

A more recent review by Swain, Hancock, Dixon, and Bowman (2015) examined the utility of ACT in the treatment of childhood problems, and identified five chronic pain studies. The authors reported consistent improvements in functional disability and pain interference for young people with chronic pain, however, they noted that author bias could not be ruled out given that one research group had conducted the majority of the studies. The authors also included case studies, and rated most of the pain studies as below average. Therefore, there is merit in re-evaluating these findings with updated studies. Wicksell, Kanstrup, Kemani, Holmström, and Olsson (2015) and Pielech et al., (2017), also provide overviews of ACT intervention studies for paediatric chronic pain, however, neither paper examines the quality of evidence.

While research has focused on evaluating the outcomes of third wave therapies, proponents of these approaches also stress the importance of examining the mechanisms through which change occurs (Hayes, Luoma, Bond, Masuda, & Lillis, 2006). Exploration of therapeutic processes enables researchers to assess whether interventions are working in accordance with their underlying theoretical assumptions, and in doing so enhance existing models (Veehof et al., 2016). Within

ACT the following six interrelated processes are promoted under the umbrella term psychological flexibility: acceptance, cognitive defusion, being present, self-as-context, values and committed actions (Hayes et al., 2006). Through increased psychological flexibility individuals have the capacity to be fully present and engage in value-directed behaviour (Hayes et al., 2006). The study of treatment processes is common within the ACT literature (Hann & McCracken, 2014), and there is a growing evidence-base demonstrating that ACT increases psychological flexibility processes, which in turn, influence changes in treatment outcomes (McCracken & Gutierrez-Martinez, 2011; Vowles, Wetherell & Sorrell, 2009; Wicksell, Olsson & Hayes, 2010).

In contrast to ACT, the mechanisms through which mindfulness interventions exert their effects are not as well established (Baer, 2009). Shapiro (2006) proposed the IAA model of mindfulness as an explanation for how the process may foster positive change. The model hypothesises that mindfulness contains three interconnected elements: intention, attention and an open and compassionate attitude (IAA). When these are simultaneously cultivated, they give rise to a shift in perspective which leads to change (Shapiro, 2006). Studies that have examined treatment processes have found mindfulness skills to increase following mindfulness-based interventions, such as MBSR (Carmody & Baer, 2008; Gaylord et al., 2011; Schmidt et al., 2011). Increases in mindfulness have also been found to precede changes in perceived stress (Baer, Carmody & Hunsinger, 2012), and to mediate the effect between mindfulness home practice and changes in well-being (Carmody & Baer, 2008).

Objectives

This review aimed to extend the work of Swain et al. (2015) by evaluating the effectiveness of acceptance and mindfulness-based interventions specifically with young people with chronic pain. Given the stage of research within the field, the review primarily focused on within-group effects. Based on the PedIMMPACT outcome domain recommendations for paediatric pain trials (McGrath et al., 2008) pain intensity, disability, anxiety and depression were included as primary outcomes for the review, as was quality of life. Secondary aims of the paper were (1) to explore

changes in acceptance and mindfulness-based intervention processes following treatment and (2) to examine how these approaches compare to control conditions.

Methods

Protocol

The protocol for this review was registered with PROSPERO and is available by following the link https://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42017053509.

Criteria for inclusion and exclusion

Population

Studies were included if they were based on a paediatric sample with a mean age of ≤18 years. This cut-off was chosen to ensure a focus on children and adolescents, while also being mindful of the ongoing debate regarding the period of adolescence and varying age limits of paediatric services around the world, some of which go up to 25 years of age.

Studies were only suitable for inclusion if they targeted chronic pain conditions (continuous or recurrent) lasting 3 months or longer. Only conditions where pain is a central feature were considered, such as headaches, musculoskeletal pain, recurrent abdominal pain and neuropathic pain. Pain associated with life-limiting conditions (e.g. cancer) or other conditions (e.g. diabetes) were excluded.

Type of studies

As the primary focus of the review is the within-group effect of acceptance and mindfulness-based interventions, studies were eligible if they utilised a pre-post/follow-up design or reported on within-subjects effects within a randomised controlled trial or non-randomized study. Both published and unpublished studies were included. Case studies, review articles and evaluations without quantitative analysis were excluded, as were non-English studies.

Intervention

Interventions which promoted acceptance and mindfulness as core treatment processes were eligible. This included ACT, MBSR, MBCT, and adaptations of these therapies for paediatric pain populations. Studies examining meditation interventions, such as qigong or yoga, without explicit reference to acceptance or mindfulness were excluded. Interventions delivered in individual or group formats were accepted.

Outcomes

Primary outcomes were pain intensity, disability, quality of life, anxiety and depression. Secondary outcomes were acceptance, mindfulness and other measures of psychological flexibility. Only self-reported measures were considered.

Search strategy

Electronic database search

An electronic search of databases was conducted in December 2016. The following databases were searched using the search terms (pain OR headache OR fibromyalgia) AND (mindful* OR meditate* OR MBCT OR MBSR OR acceptance) AND (pediatric* OR paediatric* OR adolescen* OR child* OR teen OR youth) within the title, abstracts and keywords domains:

- PsychINFO (1806-2016 Nov Week 4)
- Embase Classic and Embase (1947-2016 Week 49)
- Epub Ahead of Print, In-Process and Other Non-Indexed Citations, Ovid Medline(R) Daily and Ovid Medline (R) (1946-present)
- CINAHLplus (1937-2016 Week 49)
- Applied Social Sciences Index and Abstracts (ASSIA) (1987-2016 Week 49)
- ProQuest Dissertations and Theses Global (1997-2016 Week 49)
- ERIC (1966 -2016 Week 49)
- Cochrane Central Register of Controlled Clinical Trials (Up to December 2016)
- Open Grey (Up to December 2016)

Other sources

- *Special Interest Groups (SIG)*: A request for any unpublished studies was posted on three relevant SIGs' communication boards of the Association for Contextual Behavioural Science (ACBS) website.
- *Experts*: Three experts in the field were contacted to ask whether they were aware of any unpublished studies that would be suitable.
- *Reference lists*: The reference lists of all included studies were checked for additional studies.

Data extraction

The following data were extracted using a form specifically designed for the study: lead author, publication date, study design, inclusion/exclusion criteria, pain population, sample size, age, gender, intervention type, format and duration, therapist characteristics, fidelity procedure, follow-up period, attrition rates, outcome measures, statistical analysis and results, and adverse events. If effect sizes were calculated these were extracted. When effect sizes were not reported they were calculated by the first author. All effect sizes were converted to Cohen's *d* for ease of comparison. Five authors were contacted for additional information, of whom three replied.

Assessment of quality of included studies

Given the current review's focus on within-group effects it was deemed necessary to develop a set of quality criteria which could adequately address the primary research question. The Psychotherapy Outcome Study Methodology Rating Form (POMRF; Öst, 2008) was adapted to develop appropriate quality criteria in line with recommendations by the Centre for Reviews and Dissemination (CRD, 2008). The complete set of criteria and scoring method can be found in Appendix B. The first author assessed the quality of all included studies. Five papers (55%) were also reviewed by a second rater (3rd year Clinical Psychology doctorate student). Interrater reliability was adequate ($\kappa = 0.88$). Where differences in ratings arose, these were discussed and a consensus agreed upon.

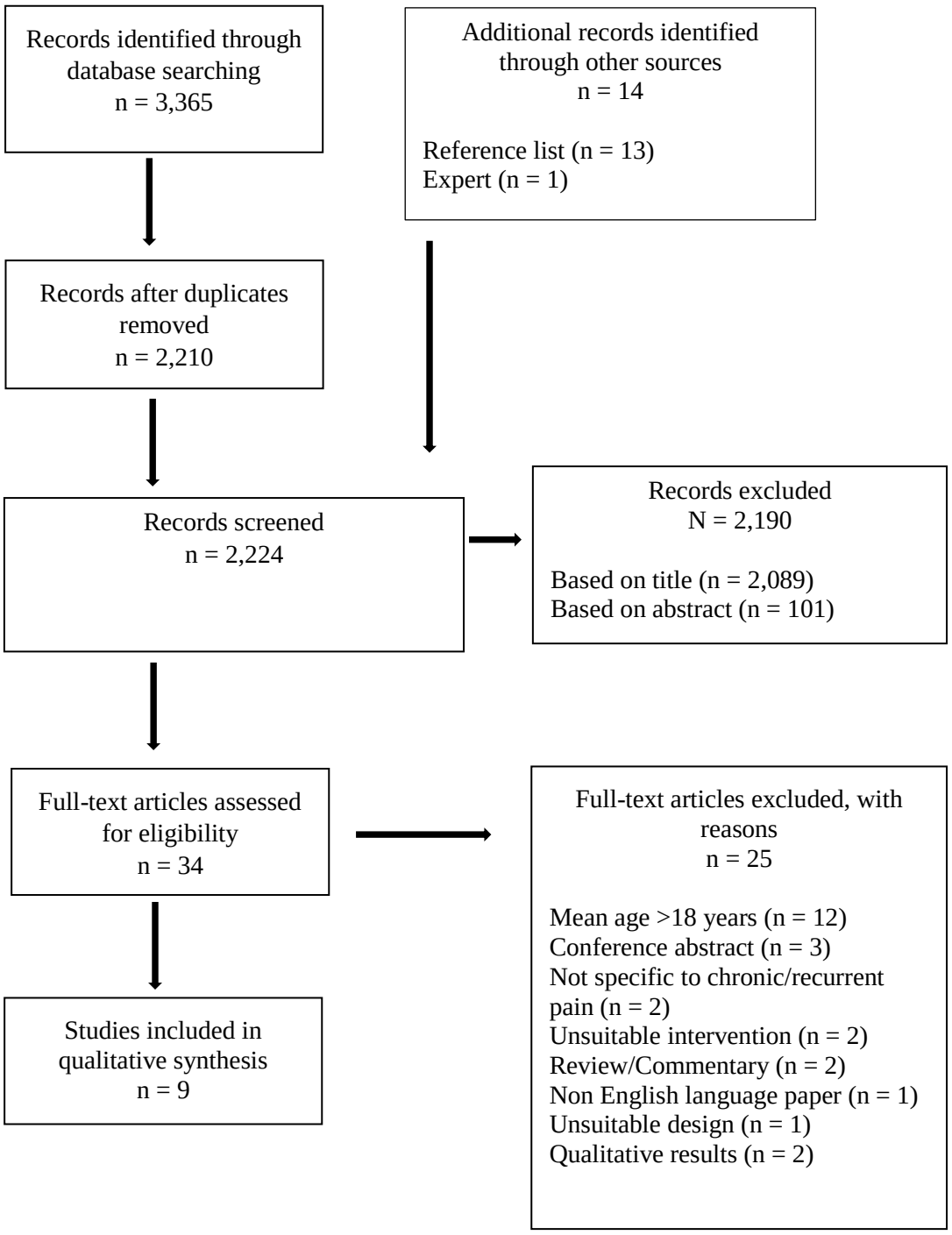

Figure 1: Flow diagram of the literature search process

Data synthesis

A narrative synthesis of the results was deemed more appropriate than a meta-analysis. This was due to heterogeneity in the types, formats and lengths of the interventions examined, the outcomes measured and the assessment periods used (post-intervention versus follow-up), which, coupled with small sample sizes, would likely have rendered the data insufficient and too heterogeneous for a meta-analysis.

Results

The search strategy returned 2,224 results, from which 9 studies met the inclusion criteria for the review. This included 7 studies found through the database search, one discovered by examining the reference lists of included studies, and one recommended by an expert in the field (see figure 1).

Characteristics of included studies

Details of the study characteristics are summarised in Table 1. Nine studies were suitable for inclusion, five of which were new studies not previously included in Swain and colleagues' (2015) review. A total of 258 participants were included in the current systematic review. Eight of the studies were published studies, one (Greco, Blomquist, Acra & Mouton, 2006) was unpublished. Five of the studies utilised a within-group design, one study was a non-randomised study, while the remaining three were RCTs. However, one of these RCT studies (Kanstrup et al., 2016) compared group versus individually delivered ACT with no control condition, and pooled the data for both groups to examine the impact of the intervention. As such, it was regarded as a within-group design for the purpose of this review.

The majority of studies reported on mixed pain populations and adolescent females. Most papers evaluated small pilot studies with sample sizes under 30 participants. Seven studies investigated ACT interventions, two of which were interdisciplinary in nature. The two remaining studies involved mindfulness-based interventions adapted from MBSR, MBCT and the Mindful School Curriculum. All interventions were

provided on an outpatient basis, with the exception of Guantlett-Gilbert, Connell, Clinch, and McCracken (2012), who delivered treatment within a residential setting. The interventions were provided in both group and individual formats, and ranged in duration from 6 to 90 hours in total. Parents participated in the intervention in six studies, with most studies involving separate sessions for parents. Follow-up assessments, ranging from 1 month to 6 months, were undertaken in the majority of studies. All studies except that of Ghomian and Shairi (2014) reported rates of attrition. Programme attrition (measured post-intervention) ranged from 4% to 37.5%, with 5 out of 8 studies reporting rates ≤ 14%. Follow-up attrition rates ranged from 18% to 31% for the 5 studies which included follow-up analyses.

Quality of included studies

Quality ratings for the included studies are presented in Table 2. While direct comparison of overall quality across studies was not possible, the rating scale provided a guide to judge the general methodological strengths and limitations of studies examining within-group effects. In general, the studies were of adequate quality, with the majority of ratings on 9 out of the 12 criteria being classified as "good" or "fair". The studies by Kanstrup et al. (2016), Wicksell et al. (2009) and Gauntlett-Gilbert et al. (2012) were found to be the most methodologically robust, while that of Ghomian and Shairi (2014) was regarded as the most flawed. Nearly all the studies provided a clear description of the sample, including inclusion and exclusion criteria. The majority of studies also used psychometrically sound measures, however, three studies were limited by the lack of validated Swedish instruments. Adequate statistics were performed in most studies, however, only Kanstrup et al. (2016) and Wicksell et al. (2009) reported their results in full. All but one study involved therapists with at least adequate levels of experience. None of the included studies reported an a priori power calculation, and the majority had small samples. Only Wicksell and colleagues (2009) performed intention-to treat analyses. Furthermore, the majority of studies failed to assess the clinical significance of the intervention or report on the presence or absence of adverse events.

Table 1: Characteristics of included studies

Study	Design	Chronic pain pop.	Sample size (% female)	Age range	Mean age (SD)	Treatment	Format	Number of sessions (duration)	Follow-up	Attrition	Outcomes
Chadi et al. (2016)	RCT	Mixed pain	19 (100)	13.9-17.7	15.8 (1.1)	Adapted MBI	Group	8 session (90 mins each)	None	17%[1]	VAS PedsQL BDI-Y BAI-Y
Gauntlett-Gilbert et al. (2012)	Within-Group	Mixed pain	98 (75)	10.8-19	15.6 (1.7)	Inter-disciplinary ACT programme	Group + Parent sessions	15 days 90 hours in total	3 months	4%[1] 26%[2]	VAS BAPQ CPAQ-A
Ghomian & Shairi (2014)	NRS	Mixed pain	20 (45)	7-12	ACT: 10.6 (1.7) Control: 10.2 (1.8)	ACT	Not specified	Not specified	1.5 months & 5 months	Not specified	FDI
Greco et al. (2006)	Within-Group	FAB	15 (87)	14-18	15.7 (1.36)	ACT	Individual + 1 family education session	12-14 sessions (*m*=12.8) (60-90 mins)	1 month	12%[1] 18%[2]	FDI YQOL CDI MASC

Study	Design	Chronic pain pop.	Sample size (% female)	Age range	Mean age (SD)	Treatment	Format	Number of sessions (duration)	Follow-up	Attrition	Outcomes
Hesse et al. (2015)	Within-Group	Recurrent headache	20 (100)	11-16	14.5 (1.6)	Adapted MBI	Group	8 sessions 120 mins	None	25% [1]	PedMIDAS PedsQL CES-DC MASC CPAQ-A
Kanstrup et al. (2016)	RCT	Mixed pain	30 (80)	14-18	16 (1.6)	Inter-disciplinary ACT programme	Group/ Individual + Parent sessions	17 sessions 45 min individual and 2 hours group	None	37.5%[1]	NRS CES-DC PIPS
Martin et al. (2016)	Within-Group	NF1	10 (60)	12-20	16.9 (2.9)	ACT	Group + Parent sessions	2 sessions (3 hours) + 1 telephone booster at 4-6 weeks (15-20 min)	3 month	14%[1] 29%[2]	VAS FDI IPI CES-DC PASS 20 CPAQ-A
Wicksell et al. (2007)	Within-Group	Mixed pain	14 (79)	13-20	17 (2.1)	ACT	Individual + Parent sessions	5-29 sessions (*M* = 14.4, *SD* = 6.6)	3 months 6 months	12.5%[1] 31%[2]	NRS FDI

Study	Design	Chronic pain pop.	Sample size (% female)	Age range	Mean age (SD)	Treatment	Format	Number of sessions (duration)	Follow-up	Attrition	Outcomes
Wicksell et al. (2009)	RCT	Mixed pain	32 (78)	10.8-18.1	14.8 (2.4)	ACT	Individual + Parent sessions	10 sessions (60 min)	*M* = 3.5 months post treatment *M* = 6.8 months post treatment	9%[1] 25%[2]	VAS FDI SF-36 – physical & mental CES-DC

[1] Attrition rates at post-intervention; [2] Attrition rates at follow-up; BABQ = Bath Adolescent Pain Questionnaire; BAI-Y = Beck Anxiety Inventory for Youth; BDI-Y = Beck Depression Inventory for Youth; CDI = Children's Depression Inventory; CES-DC = Centre for Epidemiological Studies Depression Scale for Children; CPAQ-A = Chronic Pain Acceptance Questionnaire-Adolescent Version; FAP = Functional Abdominal Pain; FDI = Functional Disability Index; IPI = Impact of Pediatric Illness Scale; MASC = Multidimensional Anxiety Scale for Children; MBI Mindfulness-Based Intervention; NF1 = Neurofibromatosis type 1; NRS = Non-Randomised Study/Numerical rating Scale; PASS-20 = Pain anxiety symptoms scale-20; PedMIDAS = Pediatric Migraine Disability Assessment; PedsQL = Pediatric Quality of Life Inventory; PIPS = Psychological Inflexibility in Pain Scale; SF-36 = The Short Form-36 Health Survey; VAS = Visual Analogue Scale; YQOL = Youth Quality of Life Inventory-Revised.

Table 2: Quality ratings for included studies

Study	Sample	Protocol	Adverse events	Representativeness	Power	Therapist	Fidelity	Outcome	Statistics	Attrition	Follow-up	Clinical Sig.
Chadi et al. (2016)	Good	Fair	Poor	Poor	Poor	Good	Good	Good	Fair	Fair	Poor	Poor
Gauntlett-Gilbert et al. (2012)	Good	Fair	Poor	Fair	Poor	Good	Fair	Good	Fair	Fair	Fair	Poor
Ghomian & Shairi (2014)	Fair	Poor	Poor	Fair	Poor	Poor	Poor	Good	Fair	Poor	Fair	Poor
Greco et al. (2006)	Good	Good	Poor	Fair	Poor	Fair	Fair	Good	Fair	Fair	Fair	Poor
Hesse et al. (2015)	Good	Good	Good	Poor	Poor	Good	Poor	Good	Poor	Fair	Poor	Poor
Kanstrup et al. (2016)	Good	Good	Fair	Poor	Poor	Good	Fair	Fair	Good	Fair	Poor	Good
Martin et al. (2016)	Good	Fair	Poor	Poor	Poor	Fair	Fair	Fair	Fair	Fair	Fair	Poor
Wicksell et al. (2007)	Good	Fair	Poor	Fair	Poor	Fair	Poor	Fair	Fair	Fair	Good	Fair
Wicksell et al. (2009)	Good	Good	Poor	Fair	Poor	Fair	Fair	Fair	Good	Good	Good	Poor

Table 3: Summary of treatment effects

	Chadi et al. (2016)	Gauntlett-Gilbert et al. (2012)	Ghomian & Shairi (2014)	Greco et al. (2006)	Hesse et al. (2015)	Kanstrup et al. (2016)	Martin et al. (2016)	Wicksell et al. (2009)	Wicksell et al. (2007)
Pain intensity									
Pre - Post									
P value	$p = .07$	$p > .01$	-	-	-	$p = .35$	-	-	**$p < .01$**
Effect Size (*d*)	$d = 1.7$	$d = 0.17$[a]				$d = 0.26$[b]			**$d = 1.53$**
Pre - Follow-up									
P value	-	$p > .01$	-	-	-	-	**$p = .01$**	**$p = .004$**	**$p < .01$**
Effect Size (*d*)		$d = 0.25$					**$d = 0.51$[a]**	**$d = 1.47$[b]**	**$d = 2.37$[a]**
Disability									
Pre - Post									
P value	-	**$p < .001$**	-	**$p < .01$**	$p = .59$	-	-	-	**$p < .01$**
Effect Size (*d*)		**$d = 0.40$[a]**		**$d = 1.22$[a]**	$d = 0.08$[a]				**$d = 1.05$**
Pre - Follow-up									
P value	-	**$p < .001$**	**$p = .001$**[c]	**$p < .01$**	-	-	$p = .37$	**$p = .002$**	**$p < .01$**
Effect Size (*d*)		**$d = 0.32$**		**$d = 1.38$[a]**			$d = 0.35$[a]	**$d = 1.57$[b]**	**$d = 1.67$[a]**
Quality of Life									
Pre - Post									
P value	$p = .42$	-	-	**$p < .01$**	$p = .19$	-	-	-	-
Effect Size (*d*)	$d = .62$			**$d = 0.82$[a]**	$d = 0.49$[a]				
Pre - Follow-up									
P value	-	-	-	**$p < .001$**	-	-	$p = .17$	**$p = .01$[d]/.03[e]**	-
Effect Size (*d*)				**$d = 1.31$[a]**			$d = 0.15$[a]	**d=1.34/1.06[b]**	

	Chadi et al. (2016)	Gauntlett-Gilbert et al. (2012)	Ghomian & Shairi (2014)	Greco et al. (2006)	Hesse et al. (2015)	Kanstrup et al. (2016)	Martin et al. (2016)	Wicksell et al. (2009)	Wicksell et al. (2007)
Depression									
Pre - Post									
P value	$p = .56$	**$p < .01$**	-	$p > .05$	**$p = .009$**	**$p = .004$**	-	-	-
Effect Size (*d*)	$d = 0.39$	**$d = 0.24$**[a]		$d = 0.45$[a]	**$d = 0.67$**[a]	**$d = 0.80$**[b]			
Pre - Follow-up									
P value	-	$p > .01$	-	**$p < .05$**	-	-	$p = .52$	$p = .06$	-
Effect Size (*d*)		$d = 0.22$		**$d = 0.70$**[a]			$d = 0.06$[a]	$d = 0.94$[b]	
Anxiety									
Pre - Post									
P value	$p = .77$	**$p < .001$**	-	**$p < .001$**	$p = .32$	-	-	-	-
Effect Size (*d*)	$d = 0.19$	**$d = 0.46$**[a]		**$d = 0.67$**[a]	$d = 0.25$[a]				
Pre - Follow-up									
P value	-	**$p < .001$**	-	**$p < .001$**	-	-	$p = .98$	-	-
Effect Size (*d*)		**$d = 0.48$**		**$d = 0.87$**[a]			$d = 0.08$[a]		
Psych. Flexibility									
Pre - Post									
P value	-	**$p < .001$**	-	-	$p = .30$	**$p < .001$**	-	-	-
Effect Size (*d*)		**$d = 0.95$**[a]			$d = 0.27$[a]	**$d = 1.46$**[b]			
Pre - Follow-up									
P value	-	**$p < .001$**	-	-		-	$p = .55$	-	-
Effect Size (*d*)		**$d = 1.00$**			-		$d = 0.08$[a]		

[a] Effect size calculated by author; [b] Effect size converted to Cohen's *d;* [c] Insufficient data to calculate effect size [d] Results from SF-36 Physical Component Scale; [e] Results from SF-36 Mental Component Scale.

Within-group effects

The results of the within-group analyses are summarised in Table 3. Three studies reported post-intervention results only, while one study compared pre-intervention scores with only follow-up scores. Three studies examined changes in outcome measures at both post-intervention and follow-up, while two further studies reported on the overall effect over time (post, follow-up 1 & 2).

Primary outcomes

Pain intensity

Six studies examined the impact of acceptance and mindfulness-based approaches on pain intensity. Of the four studies that reported specifically on post-intervention changes, three found no effect (Chadi et al., 2016; Gauntlett-Gilbert et al., 2012; Kanstrup et al., 2016), while one reported large significant reductions in pain intensity (Wicksell et al., 2007). Four studies also investigated pain intensity at follow-up or across multiple time points. A significant decrease in pain intensity was observed in three of the studies (Martin et al., 2016; Wicksell et al., 2009; Wicksell et al., 2007), with effect sizes ranging from medium to large (d = 0.51 - 2.37).

Disability

Seven studies investigated changes in participants' disability scores. Three of the four studies which measured changes post-intervention reported significant reductions in disability, which were sustained at follow-up (Gauntlett-Gilbert et al., 2012; Greco et al., 2006; Wicksell et al., 2007). A further two studies observed significant changes across time (Ghomian & Shairi, 2014; Wicksell et al., 2009). Only one study (Martin et al., 2016) observed no effect at follow-up. Significant effect sizes ranged from small to large, with three of the studies reporting large effects (d = 1.05 – 1.67).

Quality of life

Changes in quality of life following the intervention were explored in five studies. Two of these reported significant improvements following the intervention (Greco et al., 2006; Wicksell et al., 2009), while three studies reported no change at either post intervention or follow-up (Chadi et al., 2016; Hesse, Holmes, Kennedy-Overfelt,

Kerr, & Giles, 2015; Martin et al., 2016). However, all three studies demonstrated a positive trend towards improved quality of life. Significant effect sizes were large (d = 0.82 – 1.34).

Depression

Five studies examined participants' depression scores post-intervention, of which three noted significant reductions (Gauntlett-Gilbert et al., 2012; Hesse et al., 2015; Kanstrup et al., 2016). Of the four studies which examined changes at follow-up, only Greco et al., (2006) reported a significant decrease in depression scores, although both Gauntlett-Gilbert et al. (2012) and Martin et al. (2016) demonstrated trends of reducing depression scores. Significant effect sizes ranged from small to large (d = 0.24 – 0.80).

Anxiety

Anxiety was explored in five studies, and included measures of both general anxiety and pain-related anxiety. Two studies observed a significant reduction in anxiety scores post-intervention, which were maintained at follow-up (Gauntlett-Gilbert et al., 2012; Greco et al., 2006). The two studies measured pain-related anxiety and general anxiety respectively, and reported effect sizes ranging from small to large (d = 0.46 – 0.87).

Treatment processes

Three studies measured changes in acceptance, while a fourth measured changes in psychological inflexibility. Kanstrup et al. (2016) reported a significant decrease in psychological inflexibility, while Gauntlett-Gilbert et al. (2012) observed increased acceptance at both post-intervention and follow-up. In both cases large effects were found (d = 0.95 – 1.46). The two remaining studies reported no significant change in acceptance levels at post-intervention and follow-up respectively (Hesse et al., 2016; Martin et al., 2016). However, the study by Hesse et al. (2016) appears to have used a non-standard scoring procedure for this outcome, and thus may not be comparable with the other results.

Acceptance and mindfulness-based approaches versus control conditions

Three studies, two of which were RCTs, compared the intervention to control conditions. Both RCTs involved random assignment of participants to conditions, although only Wicksell et al. (2009) reported an allocation concealment procedure. Both Wicksell et al. (2009) and Ghomian and Shairi (2014) found no difference between groups when compared at baseline, while Chadi et al. (2016) adjusted for baseline scores when comparing conditions. The study by Wicksell and colleagues (2009) was the only one to use a blind assessor and control for therapist effects. In light of these factors, the study by Wicksell et al. (2009) was regarded by the author as having the lowest risk of bias, while the other two studies were considered to have a high risk of bias.

The studies were mixed in terms of control conditions used. Wicksell et al. (2009) compared an ACT treatment to a multidisciplinary treatment with amitriptyline. The authors found that the ACT group reported significantly lower pain intensity (η_p^2 = .13) and higher quality of life (η_p^2 = .15) than the control group post-intervention. Both effects were medium in size. The authors observed no difference between the two groups in levels of disability or depression following the interventions. Chadi et al. (2016) compared a mindfulness-based intervention to a wait-list control condition, and found no difference in pain intensity, quality of life, anxiety or depression scores between conditions. However, the authors acknowledged that the study was not sufficiently powered to detect changes in outcomes. Finally, Ghomian and Shairi (2014) compared an ACT intervention to an unspecified control condition, and observed a significant improvement in disability scores for the ACT group post-intervention (r = 0.82), and also at one month follow-up (r = 0.75) and 5 month follow-up (r = 0.82). All effect sizes were large.

Discussion

This systematic review aimed to evaluate the effectiveness of acceptance and mindfulness-based interventions in improving outcomes for young people with chronic pain. While the primary focus was within-group effects, between-group

effects were also explored, as were proposed treatment processes. To the author's knowledge, this was the first systematic review to examine the utility of acceptance and mindfulness-based interventions with this population. As such, it expands upon previous reviews that have investigated specific third-wave interventions, such as ACT (Swain et al., 2015), or those which have looked more broadly at psychological treatments for paediatric chronic pain (Eccleston et al., 2014; Fisher et al., 2014). The fact that the majority of studies included in the review were published within the last three years points to the growing interest in third wave interventions for paediatric chronic pain.

The current review examined the impact of acceptance and mindfulness-based approaches on five primary pain outcomes. Functional disability was one of the most examined constructs, and demonstrated the most conclusive evidence in support of the effect of third wave interventions with this population, a finding also reported by Swain et al. (2015). Improvements immediately following the intervention and at follow-up were reported by all studies, except two, which both had numerous methodological limitations. The large effects observed are congruent with the goals of acceptance and mindfulness-based treatment models, which emphasise getting on with life despite one's pain; and add to the growing support for the utility of third-wave treatments in improving disability (Hann & McCracken, 2014).

Two-thirds of the studies also measured changes in pain intensity, although with more mixed results. While significant reductions were noted in three studies, two of the most rigorous studies reported non-significant findings. Such inconsistency is not surprising given that acceptance and mindfulness-based interventions do not aim to reduce symptoms. However, given that small significant improvements in pain intensity have been reported consistently in recent meta-analyses with adult samples (eg. Bawa et al., 2015; Veehof et al., 2016), the evidence suggests that this is often a by-product of such approaches if not a goal. Neuroimaging studies conducted over the last decade offer some insights into this as a number of trials have demonstrated that mindfulness meditation modulates pain perception (for a review see Zeidan, Grant, Brown, McHaffie, and Coghill, 2012).

Just over half the studies measured quality of life, and while only two reported significant improvements, the majority of effect sizes were moderate to large, and all studies demonstrated a positive trend of increasing quality of life. Seven studies examined levels of depression before and after the intervention. Results were more encouraging immediately following the intervention, with the majority of studies reporting a significant reduction in scores, including two of the most methodologically robust studies. However, significant changes were noted in only one study at follow-up, although there was general trend of reducing depression across most studies. Findings were also mixed for anxiety, however, sustained reductions were demonstrated in both pain-related anxiety and general anxiety.

Taken together these results provide some evidence for the application of acceptance and mindfulness-based interventions with young people with chronic pain, particularly, in helping them improve their physical functioning. The reported programme retention rates also indicate that participants in the majority of studies examined found these interventions to be generally acceptable. The results are largely congruent with those reported in adults reviews (Veehof et al., 2016); however, larger effect sizes were reported in the current review, which is likely due to the inclusion of so many small feasibility studies. Indeed, McCracken and Vowles (2014) noted that average effect sizes for within-group studies with adults have been in the medium to large range.

While this review demonstrated promising results, these findings should be interpreted with caution for a number of reasons. Notably, none of the studies reported an a priori power analysis, and nearly all had very small samples, making it difficult to estimate the prevalence of missed effects or spurious findings. Furthermore, although attrition was reported in nearly all the studies, only one study applied intention-to-treat analyses. Hence, the results were biased in favour of those who completed the interventions. The generalisability of the results is questionable as the studies included quite a large age range (7-20 years), and included some samples with substantial pain-related disability and distress. Due to the majority of studies involving mixed samples, it was also not possible to establish what would be most useful for specific types of pain. In addition, two of the most methodologically rigorous studies provided ACT within an interdisciplinary programme, making it

difficult to establish the unique contribution of the psychotherapeutic part of the intervention. Finally, although the overall quality of the studies was adequate in addressing the primary research question, certain biases, particularly regarding internal validity, were not addressed within the quality framework. As such, confidence in even the most consistent results is reduced in light of potential confounding variables, such as the passage of time, or therapist factors.

Some insights into the validity of the results can be gained from examining cohort studies and research with clinical populations which have assessed the course of pain during adolescence. Cohort studies examining changes in chronic pain over a one year period have reported rates of ongoing pain in participants ranging from 38% to 78% (Gaßmann, Morris, Heinrich & Kröner-Herwig, 2008; Larsson & Sund, 2005; Mikkelsson, Salminen & Kutiainen, 1997; Miro, 2009; Perquin et al., 2003). A number of cohort studies have also conducted follow-up analyses after two or three years, and have reported relatively consistent rates of pain persistence ranging from 27% - 35% (Dunn, Jordan, Mancl, Drangsholt & Le Resche, 2011; Salminen, Erkindalo, Pentti, Oksanen & Kormano,1999; Perquin et al., 2003). The study by Dunn and colleagues (2011) is particularly noteworthy as the authors assessed participants every three months for three years in order to establish more sensitive trends. They noted that the group with the worst pain trajectory was predominantly female, with the highest levels of somatisation and depression at baseline. The findings from a systematic review by Gieteling, Bierma-Zeinstra, Passchier, and Bergerand (2008) are also congruent with those noted above. The authors examined changes in recurrent abdominal pain over a period of 1 to 29 years (median 5 years) and found that 29% of participants reported pain at follow-up.

Substantially higher rates of chronic pain have been reported in studies examining the course of pain in clinical samples. For example, Karli, Bican & Zarifoğlu, (2010) observed no headache-free cases when they followed-up participants annually over four years. Similarly, Lewandowski Holley and colleagues (2013) reported no significant difference in pain ratings at 12 months follow-up. A small follow-up study to Perquin et al. (2003) assessed adolescents with different pain conditions annually for three years, and found that pain intensity and frequency, pain-related quality of life and impact of pain on family life remained stable across the three years

(Hunfeld et al., 2002). Qualitative interviews indicated that participants structured their daily activities around their pain so as not to aggravate it. This study, however, included just 14% of the original sample, and the authors noted that one of the main reasons for refusal or non-response to the study was remission of pain. It is possible, therefore, that these studies represent young people with more severe and persistent pain who access services. High rates of recurrent pain (70-71%) have also been observed in two further studies (Galli et al., 2004; Kienbacker et al. 2006), however, both studies also considered improvement rates in addition to remission rates. They reported that of those participants who continued to report pain at follow-up, 57% (Kienbacker et al. 2006) and 83% (Galli et al., 2004) described improvements in their pain.

From the above we can see that research examining the evolution of pain in adolescence has produced quite mixed findings. This is most likely due to variability in the population studied (ie. age, gender, pain condition, clinical versus cohort), and how pain is measured, including whether rates of improvement or complete remission is used as an outcome. Given that many of the studies included in this review recruited participants from tertiary pain services, which typically see more severe and enduring cases, it is probable that few would have remitted without some form of intervention. However, it is possible that an improvement in symptoms could occur naturally over time, and could account for some of the positive changes reported by the authors.

A secondary aim of the review was to explore the effectiveness of third wave therapies within controlled studies. Only three studies utilised a control condition, illustrating the preliminary stage of research within the field. Wicksell and colleagues (2009) reported significant medium effects for pain intensity and a mental health subscale of quality of life when they compared ACT to an active MDT treatment. These findings are consistent with those reported by Veehof et al. (2016), who noted significant improvements in pain and quality of life for third wave approaches when compared with MDT/relaxation interventions. Ghomian and Shairi (2014) also noted improvements in disability for an ACT group compared to an unspecified control condition, although this study had considerable methodological flaws. Finally, Chadi et al. (2016) reported no significant differences when

comparing a mindfulness intervention to a waitlist control group, however, this was possibly an artefact of insufficient power. As such, despite some promising findings no firm conclusions can be drawn regarding how acceptance and mindfulness-based treatments perform in comparison to control conditions.

A final objective within the review was to examine treatment processes. Encouragingly, most of the more recently published studies included some measure of a third-wave treatment process. Acceptance was the most studied construct, a trend also noted in the adult literature (Hann & McCracken, 2014). In contrast, mindfulness was not measured in any study, despite the availability of appropriate measures (e.g. Child and Adolescent Mindfulness Measure; Greco, Baer & Smith, 2011), albeit non pain-specific ones. Preliminary evidence for processes was somewhat encouraging as results from the two most robust studies reported large effects on measures of acceptance and psychological inflexibility. While further research is needed to assess these processes as treatment mechanisms, rather than just outcomes, the current findings indicate that acceptance and mindfulness-based interventions may operate through the same mechanisms for young people and adults alike (Scott, Hann & McCracken, 2016).

The current review had a number of strengths. Firstly, efforts were made to include non-published studies by searching grey literature, and contacting experts in the field and ACBS members. Attempts were also made to limit reporting bias by contacting authors for additional information when rating the quality of the papers. Furthermore, the review aimed to be as comprehensive as possible by addressing both outcomes recommended by PedIMMPACT, and outcomes and processes believed to be targeted by third wave treatments, as recommended by Hann and McCracken (2014). However, the review was limited in that it only included studies published in English. Due to missing data, an average correlation of 0.6 was used when computing effect sizes, so the resulting effect sizes may not be accurate. Finally, due to the small number of eligible studies, an additional analysis comparing specific treatments was not possible. Interestingly, ACT was found to be the most researched third wave treatment with this population. Veehof and colleagues (2016) noted that effect sizes were larger for all outcomes, and significantly larger for depression in ACT treatments in comparison to MBSR and MBCT. The authors speculated that the

focus on values and committed action within ACT may contribute to comparatively greater behavioural change, and account for these differences. It is possible that other researchers and clinicians in the field share this view, and see greater utility in researching and applying ACT as a treatment for paediatric chronic pain.

The findings of this systematic review provide tentative support for the supposition that acceptance and mindfulness-based interventions may be effective treatments for paediatric chronic pain, particularly for improving functional ability in adolescents. There is also evidence to suggest that these approaches may operate through some of the hypothesised mechanisms (Hayes et al., 2006), although, research in this area is very much in the preliminary stage. Finally, although it was not possible to decisively determine the efficacy of these approaches over other control conditions or treatments, the evidence available is in support of further research in this area.

The increasing popularity of third-wave treatments, demonstrated with adult populations (Graham, Gouick, Krahé, & Gillanders, 2016), and echoed in this review, is encouraging, however, significant improvements in the quality of research is imperative before firm recommendations can be made. More rigorous research, involving sufficient samples and comparisons with other active treatments, is needed to properly test the effectiveness of these interventions, while studies involving specific pain groups will help to identify what works best for whom. Confidence in reported results will also be increased by the inclusion of a priori power calculations, intention-to-treat analyses and sufficient follow-up. As the structure and format of the interventions differed substantially between the included studies, future research would benefit from conducting comparative studies in order to ascertain the optimal dosage and format (Kerns et al., 2014). Further investigations into proposed treatment processes, other than acceptance would also allow the examination of all elements of the proposed models with young people, as researchers are beginning to do with adults (Vowles, Sowden & Ashworth, 2014; Vowles, Witkiewitz, Sowden & Ashworth, 2014).

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Appendix A: Author guidelines for *Behaviour Research and Therapy*

Article structure

Subdivision - unnumbered sections

Divide your article into clearly defined sections. Each subsection is given a brief heading. Each heading should appear on its own separate line. Subsections should be used as much as possible when cross-referencing text: refer to the subsection by heading as opposed to simply 'the text'.

Appendices

If there is more than one appendix, they should be identified as A, B, etc. Formulae and equations in appendices should be given separate numbering: Eq. (A.1), Eq. (A.2), etc.; in a subsequent appendix, Eq. (B.1) and so on. Similarly for tables and figures: Table A.1; Fig. A.1, etc.

Essential title page information

• ***Title.*** Concise and informative. Titles are often used in information-retrieval systems. Avoid abbreviations and formulae where possible.

• ***Author names and affiliations.*** Please clearly indicate the given name(s) and family name(s) of each author and check that all names are accurately spelled. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower-case superscript letter immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name and, if available, the e-mail address of each author.

• ***Corresponding author.*** Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. **Ensure that the e-mail address is given and that contact details are kept up to date by the corresponding author.**

• ***Present/permanent address.*** If an author has moved since the work described in the article was done, or was visiting at the time, a 'Present address' (or 'Permanent address') may be indicated as a footnote to that author's name. The address at which the author actually did the work must be retained as the main, affiliation address. Superscript Arabic numerals are used for such footnotes.

Abstract

A concise and factual abstract is required with a maximum length of 200 words. The abstract should state briefly the purpose of the research, the principal results and major conclusions. An abstract is often presented separately from the article, so it must be able to stand alone. For this reason, References should be avoided, but if essential, then cite the author(s) and year(s). Also, non-standard or uncommon abbreviations should be avoided, but if essential they must be defined at their first mention in the abstract itself.

Graphical abstract

Although a graphical abstract is optional, its use is encouraged as it draws more

attention to the online article. The graphical abstract should summarize the contents of the article in a concise, pictorial form designed to capture the attention of a wide readership. Graphical abstracts should be submitted as a separate file in the online submission system. Image size: Please provide an image with a minimum of 531 × 1328 pixels (h × w) or proportionally more. The image should be readable at a size of 5 × 13 cm using a regular screen resolution of 96 dpi. Preferred file types: TIFF, EPS, PDF or MS Office files. You can view Example Graphical Abstracts on our information site.
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Highlights
Highlights are mandatory for this journal. They consist of a short collection of bullet points that convey the core findings of the article and should be submitted in a separate editable file in the online submission system. Please use 'Highlights' in the file name and include 3 to 5 bullet points (maximum 85 characters, including spaces, per bullet point). You can view example Highlights on our information site.

Keywords
Immediately after the abstract, provide a maximum of 6 keywords, to be chosen from the APA list of index descriptors. These keywords will be used for indexing purposes.

Abbreviations
Define abbreviations that are not standard in this field in a footnote to be placed on the first page of the article. Such abbreviations that are unavoidable in the abstract must be defined at their first mention there, as well as in the footnote. Ensure consistency of abbreviations throughout the article.

Acknowledgements
Collate acknowledgements in a separate section at the end of the article before the references and do not, therefore, include them on the title page, as a footnote to the title or otherwise. List here those individuals who provided help during the research (e.g., providing language help, writing assistance or proof reading the article, etc.)

Formatting of funding sources
List funding sources in this standard way to facilitate compliance to funder's requirements:

Funding: This work was supported by the National Institutes of Health [grant numbers xxxx, yyyy]; the Bill & Melinda Gates Foundation, Seattle, WA [grant number zzzz]; and the United States Institutes of Peace [grant number aaaa].

It is not necessary to include detailed descriptions on the program or type of grants and awards. When funding is from a block grant or other resources available to a university, college, or other research institution, submit the name of the institute or organization that provided the funding.

If no funding has been provided for the research, please include the following sentence:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Shorter communications

This option is designed to allow publication of research reports that are not suitable for publication as regular articles. Shorter Communications are appropriate for articles with a specialized focus or of particular didactic value. Manuscripts should be between 3000-5000 words, and must not exceed the upper word limit. This limit includes the abstract, text, and references, but not the title page, tables and figures.

Artwork

Electronic artwork

General points

• Make sure you use uniform lettering and sizing of your original artwork.
• Embed the used fonts if the application provides that option.
• Aim to use the following fonts in your illustrations: Arial, Courier, Times New Roman, Symbol, or use fonts that look similar.
• Number the illustrations according to their sequence in the text.
• Use a logical naming convention for your artwork files.
• Provide captions to illustrations separately.
• Size the illustrations close to the desired dimensions of the published version.
• Submit each illustration as a separate file.

A detailed guide on electronic artwork is available.

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If your electronic artwork is created in a Microsoft Office application (Word, PowerPoint, Excel) then please supply 'as is' in the native document format.
Regardless of the application used other than Microsoft Office, when your electronic artwork is finalized, please 'Save as' or convert the images to one of the following formats (note the resolution requirements for line drawings, halftones, and line/halftone combinations given below):

EPS (or PDF): Vector drawings, embed all used fonts.
TIFF (or JPEG): Color or grayscale photographs (halftones), keep to a minimum of 300 dpi.
TIFF (or JPEG): Bitmapped (pure black & white pixels) line drawings, keep to a minimum of 1000 dpi.
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Please do not:

• Supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); these typically have a low number of pixels and limited set of colors;

• Supply files that are too low in resolution;
• Submit graphics that are disproportionately large for the content.

Tables

Please submit tables as editable text and not as images. Tables can be placed either next to the relevant text in the article, or on separate page(s) at the end. Number tables consecutively in accordance with their appearance in the text and place any table notes below the table body. Be sparing in the use of tables and ensure that the data presented in them do not duplicate results described elsewhere in the article. Please avoid using vertical rules and shading in table cells.

References

Citation in text

Please ensure that every reference cited in the text is also present in the reference list (and vice versa). Any references cited in the abstract must be given in full. Unpublished results and personal communications are not recommended in the reference list, but may be mentioned in the text. If these references are included in the reference list they should follow the standard reference style of the journal and should include a substitution of the publication date with either 'Unpublished results' or 'Personal communication'. Citation of a reference as 'in press' implies that the item has been accepted for publication.

Web references

As a minimum, the full URL should be given and the date when the reference was last accessed. Any further information, if known (DOI, author names, dates, reference to a source publication, etc.), should also be given. Web references can be listed separately (e.g., after the reference list) under a different heading if desired, or can be included in the reference list.

Data references

This journal encourages you to cite underlying or relevant datasets in your manuscript by citing them in your text and including a data reference in your Reference List. Data references should include the following elements: author name(s), dataset title, data repository, version (where available), year, and global persistent identifier. Add [dataset] immediately before the reference so we can properly identify it as a data reference. The [dataset] identifier will not appear in your published article.

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List: references should be arranged first alphabetically and then further sorted chronologically if necessary. More than one reference from the same author(s) in the same year must be identified by the letters 'a', 'b', 'c', etc., placed after the year of publication.
Examples:
Reference to a journal publication:
Van der Geer, J., Hanraads, J. A. J., & Lupton, R. A. (2010). The art of writing a scientific article. *Journal of Scientific Communications, 163,* 51–59.
Reference to a book:
Strunk, W., Jr., & White, E. B. (2000). *The elements of style.* (4th ed.). New York: Longman, (Chapter 4).
Reference to a chapter in an edited book:
Mettam, G. R., & Adams, L. B. (2009). How to prepare an electronic version of your article. In B. S. Jones, & R. Z. Smith (Eds.), *Introduction to the electronic age* (pp. 281–304). New York: E-Publishing Inc.
Reference to a website:
Cancer Research UK. Cancer statistics reports for the UK. (2003). http://www.cancerresearchuk.org/aboutcancer/statistics/cancerstatsreport/ Accessed 13.03.03.
Reference to a dataset:
[dataset] Oguro, M., Imahiro, S., Saito, S., Nakashizuka, T. (2015). *Mortality data for Japanese oak wilt disease and surrounding forest compositions*. Mendeley Data, v1. https://doi.org/10.17632/xwj98nb39r.1.

Appendix B: Quality criteria

Reporting

Sample Characteristics

Good	Good description of the sample. Inclusion/exclusion criteria and all relevant demographics reported (i.e. age, gender, pain characteristics).
Fair	Adequate description of the sample. Inclusion/exclusion criteria and some demographics reported.
Poor	Vague description of the sample. Inclusion/exclusion criteria and most relevant demographics not reported.

Intervention

Good	Detailed treatment manual is available, or description of the intervention provided or referred to if published elsewhere enabling replication. Description should include duration, frequency and format of the intervention.
Fair	Adequate detail about the intervention provided, limiting replication.
Poor	Insufficient, unclear or no information about the intervention provided such that replication is not possible.

Adverse events

Good	Absence of adverse event(s) is noted.
Fair	Adverse events associated with the study are reported.
Poor	No statement about the presence or absence of adverse events provided.

External validity

Representativeness of the sample

Good	Sample is largely representative of patients seeking treatment for the disorder
Fair	Sample is somewhat representative of patients seeking treatment for the disorder (e.g. patients were excluded if the met the criteria for other major disorders)
Poor	Sample is very different from patients seeking treatment for the disorder (e.g. there are excessively strict exclusion criteria)

Power analysis

Good	A data-informed power analysis was reported and the sample size was decided accordingly
Fair	A power analysis based on estimated effect size was reported
Poor	No power analysis was reported

Internal validity – bias

Therapist experience

Good	Considerable clinical experience of the treatment (e.g practising therapist)
Fair	Some clinical experience of the treatment
Poor	Very limited experience of the treatment (e.g students) or experience not reported

Fidelity

Good	Fidelity checks were completed (e.g. weekly audio/video tapes rated by independent rater/supervisor) and fidelity considered high
Fair	Some checks were completed (e.g. independent assessment of proportion of tapes/self-rated fidelity/supervision) and fidelity considered acceptable
Poor	No checks completed or reported

Reliability and validity of outcome measures

Good	All measures have good psychometric properties.
Fair	Some, but not all measures have known or adequate psychometric properties.
Poor	Measures have unknown psychometric properties, or properties that fail to meet current standards of acceptability

Appropriate statistics

Good	Appropriate statistical techniques were used and results are reported fully (e.g. mean, standard deviation, p-values, effect sizes)
Fair	Adequate statistical techniques used but data are not fully reported
Poor	Inappropriate statistical techniques used

Handling of attrition

Good	No attrition, or proportions of attrition are described, and dropout analysis is performed, and results are presented as intent-to-treat (ITT) analysis.
Fair	Proportions of attrition are described, and dropout analysis or intent-to-treat analysis is performed
Poor	Proportions of attrition are not described, or are described but no further analysis (dropout/ITT) is performed.

Follow-up

Good	Follow-up evaluation of outcome variables completed at ≥6 months following the intervention
Fair	Follow-up evaluation of outcome variables completed between one and 6 months following the intervention
Poor	No follow up evaluation completed or reported

Clinical significance

Good	Jacobson's criteria for clinical significance was used and presented for a selection (or all) of the outcome measures.
Fair	An arbitrary criterion for clinical significance as used.
Poor	No presentation of clinical significance was done or reported.

Psychological mediators in the relationship between paediatric chronic pain and adjustment: an investigation of acceptance, catastrophising and kinesiophobia.

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Prepared in line with the guidelines for *Behaviour Research & Therapy* (see Appendix A).

Highlights

- Cognitive and contextual processes are important factors in adolescents' well-being
- Acceptance and kinesiophobia mediate effects of pain on disability and quality of life
- Catastrophising mediates the effects of pain on levels of anxiety and depression

Abstract

Background and aim: Acceptance, catastrophising and kinesiophobia have been identified within the adult literature as important processes in the relationship between pain intensity and functioning. While these constructs have received some attention within paediatric chronic pain, research is still in its infancy in understanding how these processes relate to one another and pain-related outcomes. The current study aimed to explore the mediating roles of acceptance, catastrophising, and kinesiophobia in the relationship between pain severity and adjustment.

Methods: A large sample (N = 129) of adolescents (aged 12-18 years) with heterogeneous pain conditions completed self-report measures of: pain intensity, acceptance, catastrophising, kinesiophobia, disability, anxiety, depression and quality of life once. Multiple mediation analysis was used to compare the specific mediating effects of the three processes in the relationship between pain and functioning.

Results: The current study demonstrated that acceptance and kinesiophobia partially mediated the effects of pain across measures of disability and quality of life, while catastrophising mediated the relationship between pain and emotional distress.

Conclusions: The results demonstrated that all three processes play an important role in the well-being of adolescents with chronic pain, and support emerging models, which adopt a more encompassing perspective of paediatric chronic pain.

Keywords:

Acceptance, Catastrophising, Kinesiophobia, Adolescent, Chronic Pain

Introduction

The importance of psychological processes in the development and maintenance of pain-related distress and disability is widely accepted within the literature (Roth Geisser, & Williams, 2012; Turk, Swanson, & Tunks, 2008). Research in this field has been heavily influenced by cognitive-behavioural models, which have sought to improve the effectiveness and efficiency of Cognitive-Behavioural Therapy (CBT) by gaining a greater understanding of the intervention's mechanisms. More recently, there has been increasing empirical support for Acceptance and Commitment Therapy (ACT; Hayes, Strosahl, & Wilson, 1999) and the role of contextual behavioural factors (Scott & McCracken, 2015) in chronic pain. Key processes highlighted within two particular models, the Fear Avoidance Model (Vlaeyen & Linton, 2000) and the Psychological Flexibility Model (Hayes et al., 1999), have contributed significantly to our understanding of adjustment to chronic pain within adult populations, and are worthy of further examination within the field of paediatric pain.

The Fear-Avoidance (FA) Model

The FA model, a cognitive-behavioural model developed by Vlaeyen and colleagues (Vlayen, Kole-Snijders, Boeren, & Van Eek, 1995; Vlaeyen & Linton, 2000), highlights the roles catastrophising and kinesiophobia play in promoting disability and distress in people with chronic pain. The model proposes that catastrophic appraisals of pain and its consequences lead to pain-related fears, including fears of movement and re-injury (kinesiophobia). Such thoughts and fears give rise to hypervigilance, and escape and avoidant behaviours. While such behaviours offer short-term relief, persistent inactivity and social withdrawal result in increasing functional disability and distress (Vlaeyen & Linton, 2000). The model has gained considerable popularity, likely due to its integration of cognitive, emotional and behavioural components, and its testable hypotheses, which have prompted an abundance of research into the model, and in particular the processes of catastrophising and kinesiophobia (Crombez, Eccleston, Van Damme, Vlaeyen, & Karoly, 2012). Findings from Simons and Kaczynski (2012) support the application of the model with children and adolescents, while a Delphi poll of international

clinicians and researchers working within the field, identified both pain catastrophising, and fear of re-injury as significant predictors of pain-related disability in young people (Miró, Huguet, & Nieto, 2007).

Pain Catastrophising

Pain catastrophising has emerged as a critical construct for both adults and youths. It is commonly understood as a maladaptive thinking style characterised by a magnified view of the threat of pain and one's inability to cope (Sullivan, Bishop, & Pivik, 1995). Factor analyses with both adult and youth samples have identified three major components of catastrophising: magnification, rumination and helplessness (Crombez et al., 2003; Sullivan et al., 1995). The substantial evidence base for the role of catastrophising in chronic pain adjustment in adults has been summarised in numerous reviews (Leeuw et al., 2007; Leung, 2012; Quartana, Campbell, & Edwards, 2009), and encompasses evidence from cross-sectional research (McCracken & Gross, 1993; Molton et al., 2009; Peters, Vlaeyen, & Weber, 2005); prospective studies (Khan et al., 2011), and more recently mediation studies (Wertli et al., 2014).

The evidence-base for pain catastrophising in young people is largely congruent with the adult literature. Increased pain catastrophising has been found to predict increased pain and disability (Crombez et al., 2003; Tran et al., 2015; Vervoort, Goubert, Eccleston, Bijttebier, & Crombez, 2006), elevated anxiety and depression (Eccleston, Crombez, Scotford, Clinch, & Connell, 2004), and reduced quality of life (Libby & Glenwick, 2010). While much of the evidence is cross-sectional in nature, a prospective study by Vervoort, Eccleston, Goubert, Buysse, and Crombez (2010) reported that baseline catastrophising uniquely contributed to pain and disability six months later. However, variance accounted for was small, and it only applied to those who had low pain intensity initially.

More recently, researchers have begun to explore catastrophising as a change mechanism within paediatric interventions, primarily CBT, with mixed findings. Levy et al. (2014) found that reductions in catastrophising mediated reductions in child-reported gastroenterology symptoms, but not pain intensity or parent-reported symptoms. In contrast, an RCT by Kashikar-Zuck et al. (2013), comparing CBT and

an education programme for adolescents with fibromyalgia, found that improvements in catastrophising, along with coping strategies and coping efficacy, did not mediate changes in disability or depression. Like Levy and colleagues (2014), the authors examined changes only at post-intervention and at follow-up, and concluded that more frequent assessments during treatment possibly would have provided a more sensitive test of mediation, as most gains in the mediators and outcomes occurred during the treatment phase.

Kinesiophobia

The term kinesiophobia, first coined by Kori, Miller and Todd (1990) refers to an exaggerated and debilitating fear of physical movement, stemming from a perceived vulnerability to painful re-injury. It is an established risk factor for a range of negative outcomes, such as emotional distress (Crombez, Vlaeyen, Heuts, & Lysens, 1999; Pells et al., 2007). It is a robust predictor of disability over and above other psychosocial predictors (Vlaeyen et al., 1995; Woby, Roach, Urmston, & Watson, 2005), and has been linked to reduced physical performance on objective measures, such as lifting tasks (Neblett, Hartzell, Mayer, Bradford,& Gatchel, 2016). Kamper et al. (2012) also explored the construct in a longitudinal prospective mediation analysis, and found that fear of movement partially mediated the relationship between initial pain and disability at three months follow-up.

Despite being extensively studied within a range of adult pain populations, fear of movement/re-injury has been largely neglected within paediatric chronic pain. Sil and colleagues (2015) found that adolescents with fibromyalgia had significantly higher kinesiophobia scores than healthy controls, while in a follow-up study by the same research group, the authors observed large reductions in kinesiophobia following a CBT intervention combined with neuromuscular training (Tran et al., 2017). Taken together, these results indicate that kinesiophobia is elevated in young people with chronic pain, and that this process can be successfully targeted by interventions. Evidence for the role of this construct in young peoples' well-being has also emerged since the development of the Fear of Pain Questionnaire (FOPQ-C; Simons, Sieberg, Carpino, Logan, & Berde, 2011). Specifically, activity avoidance, a central element of kinesiophobia, has been found to be strongly associated with

disability, school impairment and GP visits, when measured using the "avoidance of activity" subscale of the FOPQ-C (Simons et al., 2015; Simons et al., 2011).

Psychology Flexibility (PF) Model

Psychological flexibility is the guiding model of ACT. It is a psychological model of human behaviour, underpinned by the philosophy of functional contextualism (Hayes, Luoma, Bond, Masuda, & Lillis, 2006). Through this lens, it is hypothesised that the content of thoughts and feelings do not directly cause pain and suffering, rather the way in which an individual responds to such internal experiences can undermine their ability to engage in valued living and lead to distress (Yu & McCracken, 2016). For individuals with chronic pain, thoughts, feelings and sensations relating to their pain can dominate their behaviour and lead to narrow and unworkable patterns of responding (Scott & McCracken, 2015). To counteract this, this model promotes psychological flexibility and its six sub-processes of acceptance, being present, cognitive defusion, self as context, values, and committed action. Collectively, these processes enable an individual to persist with or change behaviour in the service of their values, in the presence of painful thoughts, feelings and sensations (McCracken and Morley 2014). There is increasing evidence that these processes can be targeted in treatment and are related to improved outcomes, including emotional and physical functioning and service utilization (Scott & McCracken, 2015).

Acceptance

A substantial proportion of the research on psychological flexibility processes has centred on the construct of acceptance. The term acceptance is often associated with resignation or surrender, however, within ACT, acceptance refers to the quality of ongoing behaviour characterised by openness and willingness (Gillanders, Ferreira, Bose, & Esrich, 2013). It has been described as the capacity to act in accordance with one's values, while mindfully embracing unwanted experiences instead of struggling to control or reduce them (McCracken & Marin, 2014). The role of acceptance in the well-being and daily functioning of people with chronic pain has been demonstrated in numerous adult studies (McCracken & Velleman, 2010; McCracken, Vowles & Eccleston, 2005; Vowles & McCracken , 2008). Furthermore,

when compared with other ACT processes, acceptance has repeatedly been found to be the strongest predictor of outcomes (McCracken & Gutiérrez-Martínez, 2011; Scott et al., 2016)

The development of the Chronic Pain Acceptance Questionnaire – Adolescent version (McCracken, Gauntlett-Gilbert, & Eccleston, 2010) has been instrumental in the examination of acceptance among young people. In their initial validation study, the authors reported that acceptance uniquely predicted emotional, physical, social, family and developmental functioning over and above age, gender and pain intensity. A further validation study by Wallace, Harbeck-Weber, Whiteside, and Harrison (2011) corroborated these findings and noted that acceptance accounted for more variance in disability than pain intensity, anxiety, depression, and self-efficacy. Further evidence comes from a large study examining acceptance and self-efficacy in youth with chronic headaches. The authors found that acceptance predicted disability, depressive symptoms and school functioning, although self-efficacy was a stronger predictor of disability (Kalapurakkel, Carpino, Lebel, & Simons, 2014). Finally, Feinstein and colleagues (2011) found that both acceptance and psychological inflexibility predicted quality of life, but only the latter predicted anxiety and health-related quality of life. Surprisingly, neither predicted disability, however, the authors acknowledged the likelihood that the study had insufficient power to detect a relationship. As highlighted in the above systematic review, paediatric acceptance and mindfulness-based intervention studies are beginning to explore treatment processes, particularly acceptance. Treatment studies by both Weiss et al. (2013) and Gauntlett-Gilbert, Connell, Clinch, and McCracken (2012) found that changes in acceptance were associated with improvements in disability, depression and pain-related anxiety.

Comparisons between the processes

Although, a number of studies have examined associations between the three variables (Huguet, McGrath & Pardos, 2011; Simons et al., 2015; Weiss et al., 2013), to the author's knowledge, no study has yet compared their respective mediating effects in the relationship between pain and well-being. Wicksell, Olsson, and Hayes (2011) examined catastrophising, kinesiophobia and two proposed ACT measures

(pain impairment and pain reactivity) as mechanisms of change following an ACT-oriented intervention. Results from the study demonstrated that only the two ACT processes mediated improvements in pain interference and depression. However, due to the small sample, the study possibly had insufficient power to detect changes in other variables. Confidence in the findings is also undermined by the use of proxy measures rather than validated ACT-specific measures. Finally, one cannot rule out the possibility that kinesiophobia and catastrophising would mediate changes in a more CBT-oriented intervention.

While more studies have sought to compare the three processes in adults, results have been mixed. Firstly, in studies comparing acceptance and catastrophising, some have found that both constructs contribute equally to treatment outcomes (Baranoff, Hanrahan, Kapur, & Connor, 2012; Vowles, McCracken & Eccleston, 2007). In other studies, acceptance has influenced changes in physical functioning, while catastrophising has impacted upon emotional distress (Esteve, Ramírez-Maestre, & López-Martínez, 2007; Gillanders et al., 2013). Meanwhile, other authors have reported that both processes predict depression, but only acceptance predicts pain interference (Craner, Sperry, Koball, Morrison, & Gilliam, 2017). Studies comparing acceptance and kinesiophobia have reported that acceptance accounted for more variance in pain intensity, depression, disability and life satisfaction (Wicksell, Olsson & Melin, 2009). When Nicholas & Asghari (2006) compared all three variables, they found that both acceptance and kinesiophobia predicted disability, while acceptance and catastrophising predicted depression.

Context of paediatric chronic pain research

Much of the research conducted with young people has involved homogeneous pain samples. For example, only 2 out of 37 studies included in a recent review by Eccleston et al. (2014) involved mixed pain groups. The remaining studies focused on specific pain groups, such as headaches or abdominal pain. While heterogeneous pain presentations are represented within ACT research, participants are often recruited from tertiary clinics (McCracken et al., 2010; Kanstrup et al., 2016; Wicksell, Melin, Lekander, & Olsson, 2009), and may only represent a subset of

young people with significant functional disability. Both of these factors may limit the generalisability of any results found.

The current study

Although research within the field is in the early stages, preliminary evidence indicates that all three processes are associated with adjustment to chronic pain in young people, and contribute to outcomes over and above pain intensity and demographic variables. However, little is known about how these processes influence the relationship between pain and functioning individually and comparatively. As such, the current study aims to address the following questions within a heterogeneous sample of adolescents with chronic pain:

1. Does acceptance, catastrophising and kinesiophobia mediate the relationship between pain intensity and pain-related outcomes (disability, quality of life, depression and anxiety)?
2. How do these processes compare when examined together in a mediation model?

Methods

Design

This multi-site study employed a quantitative cross-sectional design in order to explore the relationships between the variables of interest (see Appendix B for study protocol). This study was part of a larger Wellcome Trust funded project, which also investigated the moderating effects of parental acceptance, catastrophising and distress on adolescents' well-being.

Participants

Eligibility

Individuals were eligible for inclusion in the study if they were aged between 12 and 18 years with chronic pain lasting three months or longer, and were attending a participating paediatric outpatient service. Individuals were excluded if they had an intellectual disability.

Recruitment

Participants were recruited from the following paediatric services within four NHS boards in Scotland: chronic pain, rheumatology, gastroenterology, neurology and general paediatrics. Members of the direct care team (doctors and nurses), with knowledge of the inclusion and exclusion criteria, identified potential participants and referred them to the research team. Those interested in taking part after reading the age-appropriate information sheet (see Appendix C), completed a reply slip (see Appendix D), and were posted a pack containing age-appropriate consent forms (see Appendix E), a battery of eight questionnaires, and a stamped address return envelope. One reminder phonecall was made within two weeks of sending the questionnaire pack. Adolescents who returned their research pack received a £5 supermarket voucher for their participation. Their GP was also notified of their involvement in the study.

Measures

Participants provided their age and gender when completing the research pack, while clinical teams provided participants' primary pain diagnosis.

Pain intensity

Participants were asked to rate their average pain during the last week from 0 (no pain) to 100 (worst possible pain) using a visual analogue scale. Visual analogue scales are reported to be valid and reliable measures of pain intensity (Varni, Thompson & Hanson, 1987) and are commonly used in studies of paediatric pain (e.g. Gauntlett-Gilbert *et al.,* 2012; Wicksell et al., 2009).

Mediators

The Chronic Pain Acceptance Questionnaire – Adolescent Version (CPAQ-A) (McCracken et al., 2010)

The CPAQ-A is a 20-item self-report measure that assesses acceptance of chronic pain in adolescents. It had been adapted from an adult version, and contains two sub-scales; engagement in activity and pain willingness. Activity engagement refers to the degree to which respondents attempt to participate in activities despite experiencing pain, while pain willingness refers to the extent to which respondents

attempt to avoid or control pain. The CPAQ-A has demonstrated adequate reliability and validity among individuals with chronic pain, both in the initial validation analysis and a later confirmatory factor analysis (Wallace et al., 2011).

The Pain Catastrophising Scale – Child Version (PCS-C; Crombez et al., 2003)

The PCS-C is a 13-item self-report measure adapted from the adult Pain Catastrophising Scale (Sullivan et al., 1995). The scale measures children's negative thinking in relation to their pain. The measure has been validated in both community and chronic pain samples (Crombez *et al*., 2003).

The Tampa Scale for Kinesiophobia (TSK-11; Woby et al., 2005)

The TSK-11 is a shortened version of the 17-item Tampa Scale for Kinesiophobia (Miller, Kori, & Todd, 1991). This measure consists of two sub-scales: somatic focus and activity avoidance, although a total score can be used to assess overall fear of movement and/or (re)injury. The psychometrics of the TSK-11 have been established, with Woby et al. (2005) reporting good internal consistency, test-retest reliability, and concurrent and predictive validity. The TSK-11 has also been found to have a better model fit than the 17-item version (Roelofs et al., 2007). The measure was designed for use with adults, however, a slightly modified version has recently been used with adolescents, which has demonstrated good internal consistency ($\alpha = 0.84$) (Sil et al., 2015 as cited in Tran et al., 2017).

Outcome variables

The Functional Disability Inventory (FDI; Walker & Greene, 1991)

The FDI is a 15 item self-report measure, which assesses children's problems in psychosocial and physical functioning due to their physical health. It has been used extensively across different chronic pain conditions (Palermo & Kiska, 2005) and has demonstrated validity and reliability in paediatric populations (Claar & Walker, 2006). PedIMMPACT recommend it as a core measure of disability (McGrath et al., 2008).

The Pediatric Quality of Life Inventory (PedsQL; 4.0 Generic Core Scale; Varni, Seid and Kurtin, 2001)

The PedsQL is a 23 item measure of health-related quality of life, consisting of four subscales which assess physical, emotional, social, and school functioning. The PedsQL has been shown to have acceptable reliability and validity in paediatric pain samples (e.g., Connelly & Rapoff, 2006). Both the child (8-12 years) and adolescent (13-18 years) versions were used in this study.

The Bath Adolescent Pain Questionnaire (BAPQ; Eccleston et al., 2005)

The depression and general anxiety subscales of the BAPQ were used in the current study. Both sub-scales have been standardized for a chronic pain population, and have demonstrated reliability and validity (Eccleston et al., 2005).

Ethics

Ethical approval was obtained from an NHS ethics committee (See Appendix F), and local permission was granted by the research and development departments of all participating health boards (see Appendix G).

Power analysis

As the method of analysis used in the current study is based on regression coefficients, a power calculation for multiple regression was conducted using G*Power. Previous research (McCracken et al., 2010; Vervoort et al., 2006), has reported moderate to large relationships between the processes (acceptance and catastrophising) and outcome measures. As such, the current study sought to detect moderate effects. The following parameters were applied in calculating the effect size: a power level of 0.8 (Cohen, 1998), a significance level of 0.05, and six predictors (3 process variables, pain intensity, age and gender). The power calculation indicated that a sample of 85 participants would be required for the study. A further power calculation was conducted using the formula $N \geq 104 + m$ (where m is the number of predictors), as recommended by Green (1991), which yielded a sample size of 110 participants. The larger estimation was used as a guide.

Data management

The dataset was explored at both a case level and item level for missing data. Cases missing more than 20% of data on any scale were omitted from the final sample. In line with recommendations by Schafer (1999), all individual items were retained, as missing data did not exceed 5% on any individual item (maximum missing data = 3.7%). Within the final sample, missing items were replaced with the series (sample) mean for all scales except the PedsQL, which used the mean of participants' completed items, as per the scale's instructions. Although mean substitution has been criticised for reducing the variance of variables and their covariance with other variables (Schlomer, Bauman, & Card, 2010), this method was justified given the small percentage of missing data and the relatively large sample size. Furthermore, descriptive statistics demonstrated only minor differences in variables' means and standard deviations before and after mean substitution.

Statistical analyses

Data were analysed using SPSS version 22 and the PROCESS macro add-on (Hayes, 2012). Preliminary analyses were completed using descriptive statistics in order to test the assumptions of normality. Pearson correlations and independent t-tests, with bootstrapping, were conducted to assess the suitability of covariates and predictors in the mediation models. Simple and multiple mediation analyses, with bootstrapping (Preacher & Hayes, 2008) were used to estimate the direct effect of pain intensity on the four outcome measures, and the indirect effects mediated by acceptance, pain catastrophising and kinesiophobia.

Bootstrapping is a re-sampling procedure, whereby the data are repeatedly taken with replacement from the original sample to produce a distribution of estimates for both the total and specific indirect effects. This distribution is sorted from high to low to construct a confidence interval (CI) for the effects (Preacher & Hayes, 2008). It is a non-parametric test, which does not assume normality, unlike the Sobel test (Sobel, 1982). As recommended by Preacher and Hayes (2008), 5000 bootstrap samples were analysed in the current study to produce bias-corrected and accelerated 95% CIs. Mediation is assumed if the CI does not contain zero.

Results

Participants

Two-hundred and forty-six young people expressed interest in the study and were sent questionnaire packs. One-hundred and thirty-four adolescents (54%) returned their questionnaires, however, five participants were excluded from the analysis due

Table1: Demographic information

	n	%
Female	88	68.22
Services recruited from		
Chronic pain	34	26.36
Rheumatology	43	33.33
Neurology	38	29.46
Gastroenterology	12	9.30
General paediatrics	2	1.55
Pain conditions		
Headache	43	33.33
Musculoskeletal pain	16	12.40
JIA	12	9.30
Crohn's disease	4	3.10
Chronic pain	3	2.33
Crohn's associated arthritis	3	2.33
IBD/IBS	3	2.33
Psoriatic arthritis	3	2.33
CRPS	2	1.55
Functional abdominal pain	2	1.55
Recurrent abdominal pain	2	1.55
Ulcerative colitis	2	1.55
Other	15	11.63

IBD = Inflammatory Bowel Disease; IBS = Irritable Bowel Syndrome; JIA = Juvenile idiopathic Arthritis

to missing data. As such, data from 129 young people were used in the final analyses. Characteristics of the sample are presented in Table 1. Participants ranged in age from 12-18 years (M = 14.45, SD = 1.44). As shown in Table 1, participants were recruited from a range of specialties. Due to the heterogeneous nature of the sample, diagnoses provided by the medical teams included a mixture of medical conditions and/or pain locations. Pain sites included: the face, neck, chest, back, abdomen, hips, legs, knees and feet.

Descriptive statistics

The mean, standard deviation, range of scores and Cronbach's alpha value for each scale are presented in Table 2. Cut-off scores for the FDI (Kashikar-Zuck et al., 2011) indicate that the average score for the current sample was within the "mild" disability range (13-20), while the mean PedsQL score was indicative of impaired quality of life (Varni, Burwinkle, Seid, & Skarr, 2003). No cut-of scores are available for the BAPQ. All scales demonstrated acceptable levels of reliability (i.e. $\alpha > .7$) with the exception of the VAS, which could not be tested due to being a single item measure. The sample was regarded as being largely representative of adolescents with chronic pain based on comparisons with similar adolescent pain studies (see Table 2), although the current sample demonstrated better functioning on measures of pain, depression and kinesiophobia.

Table 2: Descriptive statistics and comparison with other chronic pain samples

	Current study sample (n = 129)					Comparative data		
Measure	Mean	SD	Min.	Max.	α	*n*	Mean	SD
VAS	53.76	26.29	0	100	-	220	60.00[a*]	20.00
CPAQ-A	40.78	14.22	5	72	.90	109	37.80[b]	13.80
PCS-C	27.81	11.67	1	52	.94	534	25.92[c]	13.40
TSK-11	26.31	7.09	11	41	.85	17	30.25[d*]	5.55
FDI	18.48	13.18	0	49	.93	109	18.9[b]	12.00
Dep.	9.77	5.28	0	24	.86	209	12.2[e*]	3.7
Anx.	10.84	5.62	1	26	.85	209	11.2[e]	4.7
PedsQL	57.55	20.50	10.87	100	.94	534	57.81[c]	17.40

[a]From Logan et al. (2008); [b]From Wallace et al. (2011); [c]From Tran et al. (2015); [d]From Sil et al. (2015); [e] From Vowles, Jordan &Eccleston (2010); *Significant difference at $p < 0.05$

Preliminary analyses

Skewness and kurtosis values, and probability-probability (P-P) plots of each scale were examined in order to assess whether the data were normally distributed. All z-scores for skewness and kurtosis can be found in Appendix Table A.1. The VAS, FDI, BAPQ-anxiety and BAPQ-depression scales had skewness z-scores greater than +/- 1.96, indicating that they were statistically different (at $p < .05$) from a normal distribution (Field, 2009). The VAS was negatively skewed, indicating that scores were skewed towards higher levels of pain intensity, while the other three scales were positively skewed, indicating a clustering of lower disability, anxiety and depression scores within the sample. Due to non-normally distributed data on these scales, bootstrapping, using 5000 re-samples, was used when conducting the subsequent analyses.

Assessment of possible covariates

Both age and gender were investigated as possible covariates. Results are presented in Table 3. Age was significantly correlated with both depression and quality of life. No gender differences were found. As such, age was included as a covariate in models testing depression and quality of life as outcomes.

Table 3: Summary of results from covariate analyses

		FDI	BAPQ-D	BAPQ-A	PedsQL
Age	*r*	.05	.11	.16	-.17
	95% BCa CI				
	Lower	-0.13	0.01	-0.05	-0.33
	Upper	0.23	0.31	0.25	-0.00
Gender	Mean difference	-0.06	-0.81	-1.55	2.61
	95% BCa CI				
	Lower	-4.79	-2.73	-3.69	-4.69
	Upper	4.57	1.18	0.63	10.00

BCa, Bias Corrected and accelerated; CI, Confidence interval.
5000 bootstrap samples

Correlational analysis

The correlation coefficients between the proposed mediators are presented in Table 4. All three variables were significantly related to each other, with acceptance being negatively correlated with both catastrophising and kinesiophobia. The correlation coefficients between the proposed mediators and the dependent and independent variables can also be seen in Table 4. Acceptance had significant negative correlations with all independent and dependent variables, except quality of life, with which it was positively correlated. Conversely, catastrophising and kinesiophobia demonstrated significant positive correlation with all variables, with the exception of quality of life, where a negative correlation was observed. These results indicated

Table 4: Pearson correlations between predictor and outcome variables

		CPAQ-A	PSC-C	TSK-11	FDI	Dep.	Anx.	PedsQL
VAS	*r*	-.36	.46	.38	.53	.49	.42	-.54
	95% BCa CI							
	Lower	-.513	.295	.217	.371	.371	.242	-.660
	Upper	-.186	.605	.526	.663	.637	.591	-.392
CPAQ-A	*r*	-	-.67	-.56	-.61	-.50	-.41	.65
	95% BCa CI							
	Lower		-.756	-.673	-.716	-.620	-.555	.528
	Upper		-.551	-.432	-.488	-.370	-.253	.749
PCS-C	*r*	-	-	.58	.56	.58	.53	-.61
	95% BCa CI							
	Lower			.431	.420	.458	.374	-.705
	Upper			.693	.671	.687	.672	-.476
TSK-11	*r*	-	-	-	.51	.45	.40	-.64
	95% BCa CI							
	Lower				.378	.305	.231	-.735
	Upper				.633	.586	.552	-.530

BCa, Bias Corrected and accelerated; CI, Confidence interval.
5000 bootstrap samples

that all three potential mediators were associated with both pain intensity and important adjustment outcomes in the theoretically expected directions, and thus, were suitable for inclusion in the mediation analyses.

Simple mediation analyses

In order to test whether the three process variables were mediators when no competing factors were included, three simple mediation analyses were conducted for each of the four outcome measures. All three process variables partially mediated the relationship between pain intensity and each of the pain outcomes (see Appendix Table A.2.).

Multiple mediation analyses

The three process factors were also tested together in four multiple mediation models in order to test their overall indirect effect and their unique contributions in mediation. The results of these analyses are presented in Table 5, and demonstrate the direct effect of pain intensity versus the indirect effect of the three processes for each outcome, and the specific indirect effects of each mediator. Visual representations of the four models can also be found in Appendices Figure A.1-A.4.

Disability

When disability was examined as an outcome, both the direct effect and indirect effect were significant, indicating that partial mediation had occurred. The addition of the three mediators also increased the amount of variance accounted for in disability from 28% to 51%. When the specific contributions of the three process variables were tested, both acceptance and kinesiophobia were significant mediators in the relationship between pain and disability. Although the overall product of coefficient's indirect path for the mediating effect of kinesiophobia was significant, the b path (between kinesiophobia and disability) was non-significant, therefore this finding should be interpreted with some caution.

Anxiety

Partial mediation also occurred when anxiety was investigated as the dependent variable, and once again, the addition of the three processes increased the amount of

variance explained in anxiety from 18% to 33%. When the individual mediators were compared, however, only catastrophising was a significant mediator.

Depression

When depression was examined as an outcome, both the direct effect of pain and the indirect effect of the three mediators were significant. The amount of variance explained by the model also increased from 27% to 46%. Like anxiety, only catastrophising was identified as a significant mediator.

Quality of Life

Partial mediation also occurred when quality of life was tested, and the percentage of variance explained by the model increased from 32% to 62% with the inclusion of the mediators. Both acceptance and kinesiophobia were found to significantly mediate the relationship between pain and quality of life.

Pairwise contrast of specific indirect effects were produced for each model, however, none of these were significant, indicating that no mediator had a statistically stronger individual effect over the other mediators.

Table 5: Multiple mediation analyses results for chronic pain adjustment

	Beta	**Standard Error**	**95% BCa CI**	
			Lower	**Upper**
Disability				
Total effect	0.27	0.04	0.19	0.34
Direct effect	0.15	0.04	0.08	0.22
Indirect effect	0.11	0.03	0.06	0.18
Individual mediators				
Acceptance	0.06	0.03	0.02	0.13
Catastrophising	0.02	0.03	-0.03	0.08
Kinesiophobia	0.03	0.02	0.00	0.07
Anxiety				
Total effect	0.09	0.02	0.06	0.13

	Beta	Standard Error	95% BCa CI	
			Lower	Upper
Direct effect	0.05	0.02	0.01	0.08
Indirect effect	0.05	0.01	0.02	0.08
Individual mediators				
Acceptance	0.00	0.01	-0.01	0.02
Catastrophising	0.03	0.01	0.01	0.06
Kinesiophobia	0.01	0.01	-0.01	0.03
Depression				
Total effect	0.10	0.02	0.07	0.13
Direct effect	0.05	0.02	0.02	0.08
Indirect effect	0.05	0.01	0.02	0.07
Individual mediators				
Acceptance	0.01	0.01	-0.00	0.03
Catastrophising	0.03	0.01	0.02	0.06
Kinesiophobia	0.00	0.01	-0.01	0.02
Quality of Life				
Total effect	-0.42	0.06	-0.53	-0.31
Direct effect	-0.21	0.05	-0.30	-0.11
Indirect effect	-0.21	0.05	-0.32	-0.13
Individual mediators				
Acceptance	-0.09	0.03	-0.16	-0.03
Catastrophising	-0.05	0.03	-0.12	0.01
Kinesiophobia	-0.08	0.03	-0.15	-0.03

BCa, Bias Corrected and accelerated; CI, confidence interval
5000 bootstrap samples

Discussion

The purpose of the current study was to investigate the influence of two cognitive processes (catastrophising and kinesiophobia) and one contextual behavioural process (acceptance) on the relationship between pain and psychological adjustment for adolescents with chronic pain. To the author's knowledge, this is the first study to examine the relative mediating effects of these processes within a paediatric pain population.

Firstly, the results demonstrated that all three processes were significantly related in theoretically anticipated directions, such that kinesiophobia and catastrophising were positively correlated, while acceptance was negatively related to both (Simons et al., 2015; Weiss et al., 2013). Furthermore, all three processes were significantly correlated with pain intensity and the four outcome measures; greater acceptance was associated with increased quality of life, and reduced pain, disability and emotional distress; while catastrophising and kinesiophobia demonstrated the opposite relationships. These findings support previous research with young people (Crombez et al., 2003; McCracken et al., 2010; Simons et al., 2011).

The results also demonstrated the mediating effects of the three processes. When examined individually, in simple mediation models, all three processes partially mediated the effects of pain intensity on disability, anxiety, depression and quality of life. When examined together in a multiple mediation model, partial mediation was once again observed, however, certain individual indirect effects became non-significant in the presence of other mediators. Specifically, acceptance and kinesiophobia significantly mediated the effects of pain on disability and quality of life, while catastrophising was a significant mediator in the relationship between pain and emotional distress. Moreover, while acceptance and kinesiophobia appeared equal in their effects on quality of life, the results suggested that acceptance may have been a stronger mediator of disability, as it had a higher point estimate of specific indirect effect and a 95% CI further from zero. Indeed, future examination of kinesiophobia is advisable given the non-significance of the *b* pathway in predicting disability, and the proximity of the lower CI to zero.

The addition of the three processes substantially improved the variance explained by the model in all four outcomes, however, unlike previous studies (Gillanders et al., 2013), the direct effect of pain intensity remained significant in each model. This finding alligns with other studies, which have demonstrated the influence of pain intensity on well-being when controlling for psychosocial factors (Feinstein et al., 2017). Although, Feinstein and colleagues (2017) noted that pain intensity was an important predictor for both adolescents and adults, other authors have noted that the use of coping strategies in response to pain increases with age, as cognitive and emotional resources develop (Brown, O'Keeffe,Sanders, & Baker, 1986; Garnefski, Legerstee, Kraaij, Van Den Kommer, & Teerds, 2002). As such, the relevance of pain intensity in the current study may reflect a lack of maturation of coping skills. However, as this was not tested in the current study, no conclusions can be drawn.

The identification of specific indirect effects for all three processes support the hypotheses proposed by both the PF model and the FA model. Specifically, it confirmed the important influence of acceptance on quality of life (Feinstein et al., 2011), and disability (McCracken et al., 2010; Weiss et al., 2013). Similarly, it supports studies proposing that pain-related fears and subsequent avoidance of activities lead to increased disability and decreased quality of life (Vlaeyen and Linton, 2000). Although both constructs emphasise the importance of avoidance in determining how well a person adjusts to their pain, they differ in how they conceptualise it. Acceptance refers to a whole class of behavioural processes (i.e. situational, emotional, cognitive avoidance) that are likely to influence outcomes across different contexts, whilst kinesiophobia is more limited in scope as it only refers to situational avoidance. This more encompassing view may account for the stronger mediating effect of acceptance on disability.

The results also support the well-established link between catastrophising and anxiety (Crombez et al., 2003; Mano et al., 2012). Indeed, the strong association between these two constructs has prompted some authors to question whether the two are distinct from one another (Eccleston, Fisher, Vervoort, & Crombez, 2012). Recent evidence, however, would indicate that while they overlap conceptually, particularly in their shared focus on somatic symptoms, that they are statistically distinct from one another, and have unique roles in chronic pain (Tran et al., 2015).

Similar claims of redundancy have been levelled at catastrophising with respect to depression (Sullivan & D'Eon, 1989), although, numerous studies have also demonstrated its unique influence on pain and disability over and above depression (Tripp et al., 2006).

The current study expanded upon previous research which has focused on the three processes' individual contribution to adjustment, and has examined their comparable mediating roles in the relationship between pain intensity and functioning. To this end, the findings support those of Esteve et al. (2007), who found that acceptance influenced functional status and impairment, while catastrophising determined anxiety. They are also consistent with results reported by Gillanders et al. (2013), who found that acceptance was a significant mediator of physical functioning, while catastrophising was a significant mediator of emotional functioning.

Taken together the results of the current study, combined with those of Gillanders et al. (2013) and Esteve et al. (2007), suggest a delineation between more behaviourally-oriented processes and outcomes, and more cognitive/emotional ones. However, it is likely that the process of adjustment is more complex and involves both contextual and cognitive factors (Gillanders et al., 2013). Recently, some authors have begun to explore the interaction between these factors. For example, the communal coping model of pain catastrophising (Sullivan, 2012) argues that the social context is a critical determinant in the relationship between pain catastrophising and adjustment, and proposes that catastrophising serves a communicative function to elicit care and support. Similarly, Vowles, McCraken and Eccleston (2008) proposed that the influence of thinking processes on behaviour is situationally determined, and demonstrated that acceptance mediates the effect of catastrophising on functioning. This perspective was applied by Gillanders and colleagues (2013) when reflecting upon their finding that acceptance did not uniquely mediate emotional functioning; a finding replicated in the current study. The authors concluded that, although the level of acceptance may impact upon the degree to which catastrophising effects emotional distress, the shared variance between the two constructs may inhibit any unique contribution of acceptance (Gillanders et al., 2013).

Strengths and limitations

The study had a number of strengths. Firstly, it involved a large sample, unlike many studies in the field, as highlighted in the above systematic review. It was also representative in terms of pain conditions, and spanned a large geographical area within Scotland. There was strong theoretical and empirical justification for the processes under scrutiny, and these were examined within multiple mediation models, which enabled the author to compare the relative size of effect mediated by each variable, and in doing so, compare the underlying theories (Preacher & Hayes, 2008). Furthermore, investigating multiple mediators at once reduced the risk of parameter bias, which can occur when other important variables are omitted from the analysis (Preacher & Hayes, 2008). Finally, the multiple mediation approach used (Preacher and Hayes, 2008) has the advantages of directly testing the indirect effect.

The findings of the current study must also be considered in view of a number of limitations. Of note, this study was cross-sectional in nature, and as such, no conclusions can be inferred regarding causality. While the models were determined on theoretical grounds, the variables undoubtedly have reciprocal relationships. Furthermore, although the heterogeneous nature of the sample increases the representativeness of the findings, it also potentially limits their application to specific pain groups. In addition, the results may not generalise to children under 12 years of age with chronic pain, as research has demonstrated age-related differences in the relationships between the variables investigated (Feinstein et al., 2017; Tran et al., 2015). The use of postal questionnaires also potentially skewed the results towards those better adjusted, and may account for the relatively low disability scores within the sample. While nearly all the scales in the study have been validated with paediatric samples, they are all self-report measures. Future studies would benefit from using more objective measures of overt functioning. This would allow for the more accurate measurement of these constructs, and could potentially reduce the amount of variance shared between them. Many of the measures were also derived from adult scales, and therefore may neglect important development components unique to young people (Eccleston, Jordan and Crombez, 2006). Indeed, chronic pain is widely accepted as a biopsychosocial phenomenon, and as such, the influence of social and environmental factors should not be ignored (Miro et al.,

2007). The wider project, of which this study is a part, aims to address this to some degree by considering the moderating effects of parental factors.

Implications for research and practice

Future research should seek to address some of these shortfalls cited above by considering a more encompassing perspective, which considers intrapersonal, interpersonal and environmental factors, and how these processes interact to influence outcomes. Examination of other psychological flexibility processes within paediatric chronic pain is also needed in order to ascertain the utility and validity of all components of the PF model with this population (Scott & McCracken, 2015). However, for this to be achieved, the field must follow in the footsteps of the adult literature, and expand the range of ACT process measures available for paediatric populations, particularly those with chronic pain (Pielech, Vowles & Wicksell, 2017). In order to establish the temporal relationships between the variables, future research would benefit from longitudinal designs and the measurement of processes at multiple time points, including during treatment for intervention studies (Kazdin, 2007). Research with adults has begun to examine changes in ACT processes more sensitively through the use of weekly diaries (Vowles, Fink & Cohen, 2014). Adoption of similar designs would greatly improve our knowledge of change mechanisms within intervention studies (Kazdin & Nock, 2003).

For clinical practice, these results highlight the potential benefit in targeting these three processes in young people presenting with pain-related disability and distress. As previously mentioned, catastrophising and kinesiophobia are both cognitive processes typically addressed in CBT, while increased acceptance is a key goal of ACT. Although these two treatments differ in their theoretical underpinnings, there is considerable overlap in therapeutic techniques, with both utilizing behavioural interventions such as exposure. This shared focus of functional restoration is likely to account for results demonstrating improvements in processes not directly targeted in either treatment. For example, authors within both the adult and child literature have noted improvements in catastrophising and kinesiophobia following ACT (Gauntlett-Gilbert et al., 2012; Vowles, McCracken & Eccleston, 2007; Wicksell et al., 2007), while others have observed improvements in acceptance following CBT (Baranoff et

al., 2012; Weiss et al., 2013). A meta-analysis comparing ACT and CBT reported that ACT had a greater impact on ACT processes, while no differences were observed for proposed CBT processes (Ruiz, 2012). However, the only chronic pain study within the meta-analysis did not find any difference between treatments with regards to changes in acceptance or control (Wetherell et al., 2011). These findings suggest both approaches may have utility in addressing both cognitive and contextual factors involved in adjustment to paediatric chronic pain.

In conclusion, the study demonstrated that three processes (acceptance, catastrophising and kinesiophobia), widely recognised for their influence on adjustment within the adult literature, also play significant roles in the well-being of adolescents with chronic pain. A comparison of these processes indicated that both acceptance and kinesiophobia were important determinants of disability and quality of life, while catastrophising was a significant mediator in the effects of pain on emotional distress. Although the use of a cross-sectional design may have impeded a more sensitive comparison of these processes, emerging perspectives support a more integrative view of the constructs. Therefore, future research should endeavour to explore the interconnections between these processes and pain related outcomes to advance the field.

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Appendix A: Author guidelines for *Behaviour Research and Therapy*

Article structure

Subdivision - unnumbered sections

Divide your article into clearly defined sections. Each subsection is given a brief heading. Each heading should appear on its own separate line. Subsections should be used as much as possible when cross-referencing text: refer to the subsection by heading as opposed to simply 'the text'.

Appendices

If there is more than one appendix, they should be identified as A, B, etc. Formulae and equations in appendices should be given separate numbering: Eq. (A.1), Eq. (A.2), etc.; in a subsequent appendix, Eq. (B.1) and so on. Similarly for tables and figures: Table A.1; Fig. A.1, etc.

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Please submit tables as editable text and not as images. Tables can be placed either next to the relevant text in the article, or on separate page(s) at the end. Number tables consecutively in accordance with their appearance in the text and place any table notes below the table body. Be sparing in the use of tables and ensure that the data presented in them do not duplicate results described elsewhere in the article. Please avoid using vertical rules and shading in table cells.

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Please ensure that every reference cited in the text is also present in the reference list (and vice versa). Any references cited in the abstract must be given in full. Unpublished results and personal communications are not recommended in the reference list, but may be mentioned in the text. If these references are included in the reference list they should follow the standard reference style of the journal and should include a substitution of the publication date with either 'Unpublished results' or 'Personal communication'. Citation of a reference as 'in press' implies that the item has been accepted for publication.

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As a minimum, the full URL should be given and the date when the reference was last accessed. Any further information, if known (DOI, author names, dates, reference to a source publication, etc.), should also be given. Web references can be listed separately (e.g., after the reference list) under a different heading if desired, or can be included in the reference list.

Data references

This journal encourages you to cite underlying or relevant datasets in your manuscript by citing them in your text and including a data reference in your Reference List. Data references should include the following elements: author name(s), dataset title, data repository, version (where available), year, and global persistent identifier. Add [dataset] immediately before the reference so we can properly identify it as a data reference. The [dataset] identifier will not appear in your published article.

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Van der Geer, J., Hanraads, J. A. J., & Lupton, R. A. (2010). The art of writing a scientific article. *Journal of Scientific Communications, 163,* 51–59.
Reference to a book:
Strunk, W., Jr., & White, E. B. (2000). *The elements of style.* (4th ed.). New York: Longman, (Chapter 4).
Reference to a chapter in an edited book:
Mettam, G. R., & Adams, L. B. (2009). How to prepare an electronic version of your article. In B. S. Jones, & R. Z. Smith (Eds.), *Introduction to the electronic age* (pp. 281–304). New York: E-Publishing Inc.
Reference to a website:
Cancer Research UK. Cancer statistics reports for the UK. (2003). http://www.cancerresearchuk.org/aboutcancer/statistics/cancerstatsreport/ Accessed 13.03.03.
Reference to a dataset:
[dataset] Oguro, M., Imahiro, S., Saito, S., Nakashizuka, T. (2015). *Mortality data for Japanese oak wilt disease and surrounding forest compositions*. Mendeley Data, v1. https://doi.org/10.17632/xwj98nb39r.1.

Appendix B: Study protocol

Research Proposal

Title: An investigation of the mediating roles of psychological inflexibility, catastrophizing and kinesiophobia in the relationship between pain experience and adjustment to paediatric chronic pain.

Introduction

Paediatric chronic pain is a prevalent and significant health condition, often accompanied by substantial personal and economic costs. Chronic pain can be persistent or recurrent, and is typically defined as pain lasting more than three months (Merskey & Bogduk, 1994). The prevalence of paediatric chronic pain has been estimated at approximately 25% (Perquin *et al.*, 2000), although a recent systematic review observed considerable variation in prevalence rates ranging from 4-88% (King *et al*., 2011). Consistent findings from epidemiological data include higher rates of chronic pain among females, increasing prevalence of pain with age, and the most frequent recurrent pains being headaches, abdominal pain, musculoskeletal pain and pain combinations (King *et al.* 2011). Research would also indicate that prevalence rates are increasing (Bandell-Hoekstra *et al.,* 2001).

Paediatric chronic pain is a serious and complex health concern that can interfere with the daily functioning and developmental trajectory of young people. The impact of pain is widespread and variable. For example, Eccleston and Clinch (2007) would argue that the majority of young people who report chronic pain do not experience extensive distress and disability. The authors cite the large epidemiological study by Perquin *et al*. (2000), which reported that although approximately 8% of the sample experienced episodes of severe pain they were still attending school, a strong indicator of adjustment.

There is a significant proportion, however, who do report impaired functioning and quality of life for both themselves and their families. This is particularly true for those attending pain clinics. Among this population it is common for young people to miss substantial amounts of school days, experience mood problems and withdraw from activities (Palermo, 2000). Sleep disturbance is another frequently cited problem (Palermo & Kiska, 2005), as is an elevated risk of developing internalising symptoms in response to the pain, such as phobias (Palermo, 2000). Furthermore, there is evidence that these debilitating effects in youth may continue into adulthood (Walker *et al.,* 1998).

Mechanisms of adjustment

Given the array of negative consequences often associated with paediatric chronic pain, it is important for researchers and clinicians to understand the processes which contribute to these impairments, so that they can be addressed. The link between pain severity and impairment has been well documented in the literature (e.g. Claar & Walker, 2006), and offers some explanation for why individuals adjust to their pain differently. However, evidence from both adult and child studies indicate that other factors may play an important role in the process. Indeed, our understanding of the mechanisms by which pain may lead to adjustment problems is gradually increasing. Three variables to emerge from the adult literature which may illuminate the complex relationship between pain experience and maladjustment are catastrophizing, kinesiophobia and psychological inflexibility.

Catastrophizing and kinesiophobia

Pain catastrophizing is characterised by a magnified view of the threat of pain and one's inability to cope with it (Tran *et al.*, 2015). Kinesiophobia is a fear of movement and/or (re)injury, which typically develops in response to movement-related pain or disability (Pells *et al.*, 2007).

Both catastrophizing and kinesiophobia have been widely conceptualised as linking pain and maladjustment through the cognitive-behavioural Fear-Avoidance Model. The model asserts that painful stimuli can lead to catastrophic thoughts about the harmfulness of pain. Such thoughts may generate fear about pain associated with certain movements, making the individual more likely to avoid such activities. This pattern of avoidance can then result in disability over time (Simons & Kaczynski, 2012).

Both variables are among the leading psychological factors known to contribute to pain chronicity and are associated with various dimensions of functional disability in adult chronic pain populations (e.g. Arnow *et al.*, 2011; Roelufs *et al.*, 2004). Interventions targeting these processes, such as CBT and multidisciplinary treatments, have observed improvements in outcomes, such as quality of life and functional disability following treatment (Monticone *et al*., 2014)

Simons & Kaczynski (2012) recently investigated the fear-avoidance model in a paediatric pain population, and observed that both catastrophizing and fear of pain predicted disability. While the role of catastrophizing in paediatric adjustment to pain has been well documented (e.g. Crombez *et al.*, 2003), fear of movement has been largely neglected, with most studies investigating fear of pain instead.

Psychological inflexibility

The final variable of interest in the present study is a relatively new concept which has emerged out of third-wave therapies, namely Acceptance and Commitment Therapy (ACT) (Hayes *et al.*, 1999). Psychological inflexibility is the inability to act in line with one's values in the presence of unpleasant emotions, thoughts, or physical symptoms (Wicksell et al., 2010).

Psychological inflexibility is made up of six overlapping and interrelated processes. Of particular interest to the current study are the processes experiential avoidance and cognitive fusion. Experiential avoidance is the attempt to avoid thoughts, feelings and other internal experiences, and often involves engaging in maladaptive behaviours (Hayes et al., 1999). Cognitive fusion refers to the process by which individuals can become fused with their thoughts and act according to these thoughts rather than what is happening in reality (Hayes *et al.*, 1999). The other processes of dominance of the conceptualised past and feared future, and attachment to the conceptualised self refer to the processes by which people become fused with verbally based conceptualisations of the past, future, and the self. The remaining two processes refer to more overt behaviours which go against value-directed living.

These processes underpin ACT, a treatment which aims to increase functioning and quality of life by helping individuals connect with the present moment and consciously act in accordance with their values and life goals (Wicksell et al., 2015). In doing so ACT promotes the opposite of these 6 processes which collectively form psychological flexibility.

An ACT model of chronic pain proposes that individuals experience problems when they engage in activities which offer short term relief but which ultimately prevent them from living according to their values. Over time, such avoidance of difficult

psychological events results in a narrow and inflexible pattern of behaviour, or psychological inflexibility (Wicksell et al., 2010).

There are similarities between ACT and the fear-avoidance model as treatment approaches, for example, they both emphasize the role of exposure. However, there are also significant differences. Unlike cognitive-behavioural treatments based on the fear-avoidance model, which aim to correct faulty predictions and reduce pain-related fear through exposure and thought challenging, ACT does not seek to alter the content of thoughts (Wicksell et al., 2011). Rather than reducing pain-related fear it aims to promote value-directed living. As such psychological (in)flexibility, catastrophizing and kinesiophobia can be seen as related but distinct constructs.

Adult chronic pain

Empirical support for ACT and its underlying processes with adult chronic pain populations has increased rapidly over the last decade. A number of cross-sectional and prospective studies have found correlations between ACT processes, such as acceptance, mindfulness, experiential avoidance and cognitive fusion, and indicators of adjustment (e.g. McCracken & Eccleson, 2005; Mun et al., 2014). Within this population the mediating role of psychological (in)flexibility is predominantly studied as a mechanism of therapeutic change in ACT outcome studies. Results from these studies on the whole support both the effectiveness of ACT interventions and the mediating role of psychological inflexibility (Wicksell *et al*., 2010).

Paediatric chronic pain

Due to the unique developmental and contextual factors relevant in child and adolescent populations, findings from adult studies cannot be assumed to generalise to young people. To address this, a limited number of papers have examined the utility of ACT-processes and the intervention itself in paediatric chronic pain populations, and have reported findings that are largely consistent with those from adult studies.

Evidence from correlational studies investigating acceptance, through the development and validation of the Chronic Pain Acceptance Questionnaire – Adolescent version, observed that greater acceptance was associated with lower

levels of disability and distress (McCracken et al., 2010), and accounted for more variance than pain intensity, anxiety, depression, and self-efficacy (Wallace et al., 2011). A small study by Feinstein et al. (2011) reported that higher psychological inflexibility predicted higher anxiety and lower quality of life, while increases in acceptance were associated with better quality of life. In the development of the Avoidance and Fusion Questionnaire for Youth significant correlations were also observed between psychological flexibility and outcomes, including anxiety and quality of life (Greco et al., 2008). The authors also noted that the findings support experiential avoidance and cognitive fusion as distinct processes which make unique contributions to outcomes after controlling for acceptance and mindfulness.

Evidence for the use of ACT in paediatric pain has been provided by a series of clinical studies, including a case report, an open trail and the only RCT to date to the author's knowledge (Wicksell et al., 2005; Wicksell et al., 2007; Wicksell et al., 2009). A large treatment study by Logan et al. (2012) also found that an ACT-consistent intervention promoting engagement in valued activities increased willingness to engage in a self-management approach to pain, while also reducing disability, depression and improving coping. More recent evidence has been provided by a small clinical study by Ghomain & Shiri (2014) who observed improved quality of life following ACT.

Like the adult literature, researchers in this area have examined the role ACT processes play in the process of change. Intervention studies by both Weiss et al. (2013) and Gauntlett-Gilbert et al. (2013) found that changes in acceptance predicted changes in depression and disability. Wicksell et al. (2011) also examined mediators of change in which ACT and cognitive behavioural processes (kinesiophobia and catastrophizing) were included. Results indicated that only the ACT processes mediated the effects of the treatment, demonstrating that these processes are central to improvements in outcomes. The study, however, was limited by a small sample and a lack of ACT-specific measures.

While offering promising results, research into psychological (in)flexibility with paediatric chronic pain populations is limited by a number of factors. Firstly, in many of the studies sample sizes were very small, and were also often quite specific types

of pain. The lack of valid instruments has largely limited the study of ACT processes to acceptance and mindfulness only. Finally the role psychological (in)flexibility plays in relation to pain severity and maladjustment has only been explored in outcome studies and only one study has applied mediation analysis to explore this relationship.

Current study

Epidemiological findings indicate that paediatric chronic pain is extremely prevalent, can be highly debilitating and, as such, should be considered a major health concern. Continued research is needed to improve the experience and impact of this condition. Evidence among adults over the past decade supports ACT and psychological flexibility as a promising avenue in understanding and facilitating adjustment in chronic pain. Encouraging evidence is also emerging from studies involving young people, although a number of limitations undermine these findings. The current study, therefore, aims to address some of these limitations and contribute to this developing evidence base.

The current study will compare the mediating roles of catastrophizing, kinesiophobia and psychological inflexibility in the relationship between pain severity and adjustment, as measured by disability, quality of life and mood. In doing so it will build on the evidence-base of the role played by catastrophizing and contribute to the evidence-base of the less studied variables of kinesiophobia, experiential avoidance and cognitive fusion. To the author's best knowledge, this will also be the first study to compare these variables using mediation analysis with this population and to examine them as they occur naturally, rather than as processes of therapeutic change. Unlike most other studies published in this field, the current study will include a broader heterogeneous sample of young people who have been referred to a chronic pain service and those who have not but who experience pain. Identifying salient mediating factors in adjustment to pain will enable early and targeted interventions and may result in improved outcomes for young people challenged by chronic pain.

Hypotheses:

1) Catastrophizing, kinesiophobia and psychological inflexibility will mediate the relationship between pain severity and indicators of adjustment (disability, mood and quality of life).

2) Those high in psychological inflexibility, catastrophizing and kinesiophobia will report higher levels of maladjustment to their chronic pain.

Research Questions / Objectives:

2) What is the principal research question / objective? (IRAS A10)

To what degree do psychological inflexibility, pain catastrophizing and kinesiophobia mediate the relationships between pain severity and outcomes (disability, quality of life and mood) in a paediatric pain population, both collectively and individually?

3) What are the secondary research questions / objectives if applicable? (IRAS A11)

I. To ascertain the level pain, and the degree and types of functional disability in a heterogeneous sample of young people with chronic pain.

Methodology

4) Please give a full summary of your design and methodology. It should be clear exactly what will happen at each stage of the project. (Relevant to IRAS A13)

Design

A cross-sectional quantitative design will be used. Participants will complete a battery of seven self-report questionnaires relating to pain. The data will be explored using correlation, multiple regression analyses and multiple mediation analyses in order to answer the research questions.

Ethics

Ethical approval will be sought from The University of Edinburgh, School of Health in Social Science. This project will form part of a larger study funded by the

Wellcome Trust. As such, multi-site NHS research ethical approval will be sought (including Lothian, Greater Glasgow and Clyde, and Dumfries and Galloway).

Participants

Participants will be young people aged 10-18 currently attending an outpatient specialist clinic for chronic pain or a tertiary clinic for a condition where chronic pain is a central feature.

Procedure

The paediatric chronic pain service and the specialist clinics it receives referrals from will be invited to participate in this study. These clinics include rheumatology, orthopaedics, gastroenterology, neurology (headaches clinics), general paediatrics and acute pain. The researcher will then meet with the clinical team for participating services to verbally explain the study, answer any questions they may have, and provide them with an information sheet to give to potential participants.

The clinical team will be responsible for identifying potential participants and explaining the study to them. The medical team will record the details of any interested individuals who would like further information and obtain permission to forward their details onto the researcher, who will contact them with information and invite them to take part. The researcher's contact details will also be made available for any individuals not wishing to give their details, but who may want more information at a later stage. At both stages potential participants will be informed of the different methods of completing the questionnaires. These will include postal questionnaires, an online version of the battery and specified clinics which they can attend to complete the questionnaires, and where the researcher will be on hand to help. Parental consent and participant ascent will be obtained for all young people under the age of sixteen and all data collected will be completely anonymous. Participants will only be given access to the online system once the appropriate person has given their permission (e.g. parent or young person aged 16-18).

5) Please list the principal inclusion and exclusion criteria (IRAS A17-1 and A17-2)

Inclusion criteria: Aged between 10 and 18 years

Experiencing pain for three months or more

Attending a specialist clinic participating in the study for an active condition

Can speak English

Exclusion criteria: Developmental delay/learning disability

6) How will data be collected?

If quantitative, list proposed measures and justify the use of these measures. If qualitative, explain how data will be collected giving reasonable detail. (Don't just say 'by interviews')

Demographic information will be collected such as age, gender, type of pain, clinics attended. Data will also be collected using the following self-report questionnaires:

Pain intensity

Participants will be asked to rate their general pain during the last week from 0 (no pain) to 100 (worst possible pain) using a visual analogue scale. Visual analogue scales are reported to be valid and reliable measures of pain intensity (Varni, Thompson & Hanson, 1987) and are commonly used in studies of paediatric pain (e.g. Gauntlett-Gilbert *et al.,* 2013; Wicksell *et al.,* 2011). For the online version of the scale a sliding scale will be used with the same parameters. Both scales will have anchors at 0, 25, 50, 75 and 100.

Mediators

The Avoidance and Fusion Questionnaire for Youth (AFQ-Y; Greco, Lambert, & Baer, 2008)

The AFQ-Y is a 17-item questionnaire that assesses psychological inflexibility, specifically experiential avoidance and cognitive fusion. The psychometric properties of the AFQ-Y have been demonstrated in a series of large studies by Greco and colleagues (2008), and shown to good internal consistency ranging from .89 to .91 and concurrent validity, with significant relationships observed with measures of

mood, quality of life and unhelpul behavior (Feinstein et al., 2011; Greco et al., 2008).

The Pain Catastrophizing – Child version (PCS-C; Crombez et al., 2003)

The PCS-C is a 13-item self-report measure adpated from the adult Pain Catastrophizing Scale (Sullivan et al., 1995; as cited by Crombez *et al.,* 2003). The scales measures children's negative thinking in relation to their pain. The measure has been validated in both community and chronic pain samples (Crombez *et al*., 2003).

The Tampa Scale for Kinesiophobia (TSK-11; Woby et al., 2005)

The TSK-11 is a shortened version of the 17-item Tampa Scale for Kinesiophobia (Miller et al., 1991). This measure consists of two sub-scales: somatic focus and activity avoidance, although a total score can be used to assess overall fear of movement and/or (re)injury. The psychometrics of the TSK-11 have been established, with Woby et al. (2005) reporting good internal consistency, test-retest reliability, and concurrent and predictive validity. The TSK-11 has also been found to have a better model fit than the 17-item version (Roelofs et al., 2007). The measure was designed for use with adults, however, it has been used in a large clinical study of young people attending a tertiary pain clinic (Simon et al., 2011). In light of this and the fact that the author has been unable to find a paediatric measure of kinesiophobia, the current study will use the TSK-11 and validate it with a paediatric sample.

<u>Outcome variables</u>

The Functional Disability Inventory (FDI; Walker & Greene, 1991)

The FDI is a 15 item self-report measure which assesses children's problems in psychosocial and physical functioning due to their physical health. It has been used extensively across different chronic pain conditions (Palermo & Kiska, 2005) and has demonstrated validity and reliability in paediatric populations (Claar & Walker, 2006).

The Pediatric Quality of Life Inventory (PedsQL; 4.0 Generic Core Scale; Varni,et al., 2001)

The PedsQL is a 23 item measure consisting of four subscales which assess physical, emotional, social, and school functioning. The PedsQL has been shown to have reliability and validity in pediatric pain samples (e.g., Connelly & Rapoff, 2006).

The Bath Adolescent Pain Questionnaire (BAPQ; Eccleston et al., 2005)

The BAPQ subscales measuring depression and general anxiety will be used in the current study. Both scales have all been standardized for a chronic pain population, and have demonstrated reliability and validity (Eccleston et al., 2005). The scale has been used in a recent ACT intervention with young people experiencing chronic pain (Gauntlett-Gilbert et al., 2012).

Sample size

7) What sample size is needed for the research and how did you determine this? For quantitative projects, outline the relevant Power calculations and the rationale for assuming given effect sizes. For qualitative projects, outline your reasoning for assuming that this sample size will be sufficient to address the study's aims. (IRAS A59 and A60)

Previous research (e.g. Greco et al., 2008) has found moderate to large relationships between psychological inflexibility and outcome measures. In light of this, a power calculation using G*Power was conducted to detect moderate effect sizes. Guided by Cohen (1998) a power level of 0.8 was applied, and a significance level of 0.05, as is customary in psychological research. The power calculation indicated that a sample of 85 participants would be required for the study.

This calculation seems appropriate as the multiple mediation approach to be used in this study employs regression coefficients. However, multiple mediation may require a slightly larger sample. Ma and Zeng (2014) report that a sample of 100 is sufficient to detect an overall moderate mediating effect. Therefore, the current project will seek to recruit 100 participants.

8) Outline reasons for your confidence in being able to achieve a sample of at least this size. (e.g. by giving details of size of known available sample(s), percentage of

this type of sample that typically participate in such studies, opinions of relevant individuals working in that area)

The current study will be recruiting across conditions where chronic pain is a central feature, which provides a significantly larger pool to recruit from than if the study were to include only individuals attending a chronic pain service. Although it is difficult to acquire figures on the number of young people experiencing chronic pain in either Lothian or Scotland, both the rheumatology and chronic pain paediatric services at the Royal Sick Kids Hospital report that approximately 150 young people attend each of their services annually. Assuming other services, such as orthopaedics, gastroenterology and neurology have similar figures the target of 100 participants should be met.

This study will also form part of a large Scotland-wide project funded by the Wellcome Trust, which will allow the researcher to draw upon data from other NHS boards. At present Greater Glasgow and Clyde, and Dumfries and Galloway have agreed to take part.

Furthermore, creating links with support groups where individuals can find out about the study and check whether their service is participating will hopefully improve recruitment. Feedback from a paediatric chronic pain representative recently also highlighted the use of social media in a very successful research campaign, which could also be utilized in the present study.

Analysis

9) Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives. (IRAS A62)

Using the PROCESS macro add-on to SPSS, the current study will use multiple mediation analysis to investigate the influence of the three psychological processes on the relationship between pain severity and adjustment. Testing multiple mediators in one model versus in multiple simple mediation models allows one to compare the relative sizes of the effect mediated by each variable and in doing so compare the underlying theories (Preacher & Hayes, 2008). Furthermore, it reduces the risk of

parameter bias which can occur when important variables are not included in the analysis (Preacher & Hayes, 2008). Bias corrected bootstrapping will be the method used to test the total and specific indirect effects, as recommended by Preacher and Hayes (2008). Bootstrapping is a re-sampling procedure, whereby the data is repeatedly resampled to give a distribution of estimates of the indirect effect, which can be used to construct confidence intervals for the effect (Preacher & Hayes, 2008).

Management of Risks to Project

11) Please summarise the main potential risks to your study, the perceived likelihood of occurrence of these risks and any steps you will or have taken to reduce these risks. Outline how you will respond to identified risks if they should occur.

It is possible that paediatric services may not sign up to take part in the study, which would reduce the pool of potential participants. However, the project has already been positively received by two important services (chronic pain and rheumatology) and it is hoped that other services will respond likewise. In order to facilitate uptake, the researcher intends to develop a brief outline of the study and its benefits which will be circulated by the researcher's clinical supervisor, who has established links with these services. The researcher will then make herself available to attend team meetings and present the study if services agree. Participation at team meetings and regular updates will hopefully encourage teams to remain engaged in the project.

There is a risk that the study will fail to recruit the required sample size. Measures taken by the researcher to mitigate this risk include recruiting from a range of paediatric chronic conditions, creating links with local support groups and facilitating participation by providing a range of methods to complete questionnaires. The study will also be able to draw upon a larger pool of Scotland-wide data to bolster numbers, while bootstrapping will be undertaken to facilitate appropriate analysis of the data.

When using youth self-report measures there is often the risk that they will cause difficulty in terms of length and comprehension. The battery of measures intended for use in the current study were trialled with a 10 year old and found to take 30

minutes to complete. Information provided by the child's parent indicated that the child read every question very carefully and took his time, and so 30 minutes can be considered an approximate outer time limit. The language was also found to be appropriate and the few difficulties with language that were highlighted will be adapted and made more user-friendly. Finally, all the scales chosen were developed for children, with the exception of the TSK-11, however, this has been used with children with chronic pain in a recent study.

Finally, there is a small risk participants may become distressed in response to the content of the questionnaires. In order to minimise this risk child appropriate information sheets will be provided detailing the nature of the study and topics that will be addressed. It will also be made clear that they do not have to take part and can withdraw at any point.

Knowledge Exchange

12) How do you intend to report and disseminate the results of the study? (IRAS A51)

Both participants and clinical staff involved in the project will be given details for a website where the results of the study will be available. For participants unable to access the internet, other means will be offered, including a letter or a phone call. Clinical teams involved will also receive updates throughout the study in the format of newsletters and will be offered a presentation by the researcher at the end of the project, where the results and implications are outlined.

The results of the study will be written up for submission to the Doctorate in Clinical Psychology at the University of Edinburgh. The thesis will include a systematic review and a journal article which will be submitted to a relevant peer-reviewed journal (e.g. Pain).

13) What are the anticipated benefits or implications for services of the project? (E.g. If this is an NHS based project, in what way(s) is the project intended to benefit the NHS?)

Paediatric chronic pain is an expensive condition for the NHS, and with potential to be a lifelong condition for many unless effectively treated, it represents a significant

burden on NHS resources. Strong support from adult research and emerging evidence with young people indicate that there are modifiable processes impacting on how young people manage their pain. This study aims to identify the most salient processes involved in adjustment. In doing so, the study will inform treatment delivered by pain services and contribute to interventions that are specific, targeted and effective, and which lead to better outcomes. The battery of assessments used in this study may also inform the assessment battery adopted by the Lothian paediatric chronic pain service.

14) Are there any potential costs to this project?

Outline any potential financial costs to the project, including the justification for the costs (why are these necessary for the research project?) and how funding will be obtained for these costs (how will cost be met?). Please separate these into potential costs for the University and potential costs for your NHS Health board and note that you should ask your NHS Health board to meet stationery, printing, postage and travel costs.

There will be some travel costs due to travel to different sites to attend team meetings, meet with staff to explain the study and provide clinics for participants to attend to complete questionnaires. This will be limited through the use of postal questionnaires and an online system for completing the battery.

There will also be costs associated with printing and posting questionnaires. Funding for all of these will be sought from the NHS health board.

Appendix C: Information sheets

SECTION OF CLINICAL & HEALTH PSYCHOLOGY
School of Health in Social Science
Medical School
Teviot Place
Edinburgh EH8 9AG
Tel: 0131-651 3972
Fax: 0131-651-3971

Participant Information Sheet
(Young Person 12-15 years)

1. Study title

How young people cope with chronic pain: a study of psychological and social factors.

2. Invitation

You and your parent/guardian are invited to take part in a research study about pain. Before you decide if you want to take part, it is important for you to understand why the research is being done and what you will be asked to do. Please take time to read the information below carefully and discuss it with your family, friends, doctor or nurse if you wish. If you have any questions you can also contact the researcher using the contact details at the end of this sheet.

3. What is the purpose of the study?

Having chronic pain can affect lots of things in a young person's life, such as their mood, school and hobbies. Many young people are affected by chronic pain worldwide. Researchers want to find ways of improving how young people deal with their pain and improve their quality of life. We know that the way people think and feel, and the things they do when they have pain impact on how well they deal with it. This study wants to explore that further. We are also interested in how parents think and behave when their child has pain. We hope this information will help develop new treatments.

4. Why have I been invited?

Because you go to a health service for young people, and you have reported having pain in the last three months. We are hoping that around 160 pairs of young people and their parent/guardian will agree to be in this study. You can take part in this study, even if your parent/guardian does not want to take part in it.

5. Do I have to take part?

No, it is your choice whether you take part or not. If you decide to take part you are still completely free to withdraw at any time and without giving a reason. Not taking part, or withdrawing from the study WILL ABSOLUTELY NOT AFFECT the standard of care you get.

6. What will happen if I take part?

If you would like more information or wish to take part, your clinical team will ask you to fill in the attached reply slip, which gives them permission to pass along your contact details to the research team. If you would like to take part in the study you will be sent four consent forms (two for you and two for your parent/guardian), two questionnaires (one for you and one for your parent/guardian) and a stamped return envelope. Your questionnaire asks questions about your thoughts, feeling and responses to pain. Researchers will call/email your parents after one- two weeks to ensure you received the material and answer any more questions. You will be asked to sign two consent forms, keep one copy for yourself and send back your filled questionnaire and one signed consent form in the envelope provided. Your parent/guardian will include their questionnaire and one of their signed consent forms in the same stamped return envelope.

In our experience we have found that the young people's questionnaire takes about 30 minutes to complete.

When we receive your completed consent forms and questionnaires, we will send you a £5 voucher to thank you for your time and effort. Your GP will be informed about your participation in this study.

7. What else do I have to do?

Nothing will change in the services you are going to receive at the clinic.

8. What are the possible disadvantages and risks of taking part?

Some people might find some of the questions too personal or upsetting. If you find any of the questions upsetting, please feel free not to answer them.

9. What are the possible benefits of taking part?

There are no direct benefits in taking part, but, the information we get from this study may help us improve the future treatments for young people with chronic pain.

10. Who will have access to my answers/data?

All information collected about you and your parent/guardian will be kept safely protected. The questionnaire results will be anonymised by the research team and kept separate from all personal details. All data is stored in secure locations and only the research team will have access to it. Research data will be kept for 10 years, with a review then and every 5 years to decide whether it should be retained or deleted. To ensure that the study is being run correctly, we will ask your consent for authorized

people from the Sponsor and NHS Institution to look at your medical information and data collected during the study, where it is relevant to your participation in this research. The Sponsor is responsible for overall management of the study and providing insurance and protection. The research team will also inform your GP if you disclose anything that gives us reason to think you or someone else is at risk of harm.

11. Who do I speak to if problems arise?

If you have any concern about any aspect of this study please contact the researcher *Leona McGarrigle* who will do her best to answer your questions. If any harm occurs to you during this study, you can ask your parent/guardian to support you and deal with this legally.

If you have any complaints about the way in which this research project has been, or is being conducted, and wish to complain formally, please do so through the NHS Complaints Procedure. Contacts details are at the end of this leaflet.

12. What will happen to the results of the research study?

The results of the study will be presented to the clinical teams taking part in the study. They will also be published in scientific journals and presented to researchers and clinicians at conferences. You and your parent/guardian's participation will not be identified in any report/publication. If you wish to know the results of our research please let us know and we can send you a summary once the study is completed.

13. Who is organising and funding the research?

The research is co-sponsored by the University of Edinburgh and NHS Lothian and funded by the Wellcome Trust.

14. Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee. A favourable ethical opinion has been obtained from South East Scotland REC. NHS management approval has also been obtained.

15. Contacts for Further Information and Complaints

Leona McGarrigle- Trainee Clinical Psychologist – CAMHS Midlothian

Address: Eastfield Medical Centre- Eastfield Farm Road- Penicuik- EH26 8EZ

Tel: (++) 44 (0)1968 671 330 Email: s1475173@sms.ed.ac.uk

To discuss this study with some independent of the study, please contact:

Angus Macbeth- Lecturer in Clinical Psychology-

Address: Rm 1M2, Doorway 6, Medical Quad, Teviot Place, Edinburgh, EH8 9AG
Office phone: (++) 44 (0)131 6513960 Email: angus.macbeth@ed.ac.uk

To raise concerns/complaints: NHS Lothian Patient Experience Team
Waverley Gate 2-4 Waterloo Place – Edinburgh EH1 3EG
Tel: (++) 44 (0)131- 5363370 Email: feedback@nhslothian.scot.nhs.uk

SECTION OF CLINICAL & HEALTH PSYCHOLOGY
School of Health in Social Science
Medical School
Teviot Place
Edinburgh EH8 9AG
Tel: 0131-651 3972
Fax: 0131-651-3971

Participant Information Sheet
(Young Person 16-18 years)

1. Study title

How young people cope with chronic pain: a study of psychological and social factors.

2. Invitation

You and your parent/guardian are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. If there is anything that is not clear, or if you would like more information, please do not hesitate to contact the researcher on the telephone number at the end. Please take time to decide whether or not you wish to take part.

3. What is the purpose of the study?

Chronic pains affect many young people's lives worldwide. Researchers are interested in finding ways of improving how young people manage their pain and also ways of improving their quality of life. Previous research has shown that it is not just the amount of pain people have that influences how well they cope. The way people think and feel, and the things they do when they have pain also have an impact. This study aims to further explore how pain symptoms, and young people's thoughts and actions in response to pain contribute to how they are coping. The impact of parents' thoughts and behaviour will also be explored. We hope this will provide further information for the development of new treatments.

4. Why have I been invited?

Because you attend a specialist health service for young people, and have reported experiencing pain in the last three months. We are hoping that around 160 pairs of young people and their parent/guardian will agree to participate in this study.

5. Do I have to take part?

No, it is up to you to decide whether or not to take part. If you decide to take part, you are still completely free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, WILL ABSOLUTELY NOT AFFECT the standard of care you receive. You can take part in this study, even if your parent/guardian does not want to take part in it.

6. What will happen if I take part?

If you would like more information or wish to take part, your clinical team will ask you to fill in the attached reply slip, which gives them permission to pass along your contact details to the research team. If you would like to take part in the study you will be sent four consent forms (two for you and two for your parent/guardian), two questionnaires (one for you and one for your parent/guardian) and a stamped return envelope. Your questionnaire asks questions about your thoughts, feeling and responses to pain. Researchers will call/email your parents/you after one- two weeks to ensure you received the material and answer any more questions. You will be asked to sign two consent forms, keep one copy for yourself and send back your filled questionnaire and one signed consent form in the envelope provided. Your parent/guardian will include their questionnaire and one of their signed consent forms in the same stamped return envelope. In our experience we have found that the young people's questionnaire takes about 20-30 minutes to complete. When we receive your completed consent forms and questionnaires, we will send you a £5 voucher to thank you for your time and effort. Your GP will be told you are participating in this study.

7. What else do I have to do?

Participating in this research will NOT involve any changes or restrictions in your current treatment. You are encouraged to follow your treatment as prescribed by your team.

8. What are the possible disadvantages and risks of taking part?

There is a small risk participants could potentially find some of the questions too sensitive, intrusive or upsetting. If you consider any of the questions inappropriate, please feel free not to give any answer.

9. What are the possible benefits of taking part?

There is no direct benefit of taking part, however, the information we get from this study may help us improve the health care services and future treatment of patients with paediatric chronic pain.

10. Who will have access to the research records?

All information collected about you and your parent/guardian will be kept confidential. The questionnaire results will be anonymised by the research team and kept separate from all personal details. All data is stored in secure locations and only

the research team will have access to it. Research data will be kept for 10 years, with a review then and every 5 years to decide whether it should be retained or deleted. To ensure that the study is being run correctly, we will ask your consent for authorized individuals from the Sponsor and NHS Institution to access your medical information and data collected during the study, where it is relevant to your participation in this research. The Sponsor is responsible for overall management of the study and providing insurance and indemnity. Researchers will also inform your GP if you disclose anything that gives them reason to think you or someone else is at risk of harm.

11. Who do I speak to if problems arise?

If you have any concern about any aspect of this study please contact the researcher *Leona McGarrigle* who will do her best to answer your questions. If any harm occurs to you during this study, you can ask your parent/guardian to support you and deal with this legally.

If you have any complaints about the way in which this research project has been, or is being conducted, and you wish to complain formally, do so through the NHS Complaints procedure. You can find the contact details at the end of this leaflet.

12. What will happen to the results of the research study?

The results of the study will be presented to the clinical teams taking part in the study. They will also be published in scientific journals and presented to researchers and clinicians at conferences. You and your parent/guardian's participation will not be identified in any report/publication. If you wish to know the results of our research please let us know and we can share the findings with you once the study is complete.

13. Who is organising and funding the research?

The research is sponsored by the University of Edinburgh and NHS Lothian and funded by the Wellcome Trust.

14. Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee. A favourable ethical opinion has been obtained from South East Scotland REC. NHS management approval has also been obtained.

15. Contact for further information:

Leona McGarrigle- Trainee Clinical Psychologist – CAMHS Midlothian

Address: Eastfield Medical Centre- Eastfield Farm Road- Penicuik- EH26 8EZ

Tel: (++) 44 (0)1968 671 330 Email: s1475173@sms.ed.ac.uk

To discuss this study with some independent of the study, please contact:

Angus Macbeth- Lecturer in Clinical Psychology-

Address: Rm 1M2, Doorway 6, Medical Quad, Teviot Place, Edinburgh, EH8 9AG

Office phone: (++) 44 (0)131 6513960 Email: angus.macbeth@ed.ac.uk

To raise concerns/complaints: NHS Lothian Patient Experience Team

Waverley Gate 2-4 Waterloo Place – Edinburgh EH1 3EG

Tel: (++) 44 (0)131- 5363370 Email: feedback@nhslothian.scot.nhs.uk

Appendix D: Study reply slip

SECTION OF CLINICAL & HEALTH PSYCHOLOGY
School of Health in Social Science
Medical School
Teviot Place
Edinburgh EH8 9AG
Tel: 0131-651 3972
Fax: 0131-651-3971

Study Reply Slip

Project Title: How young people cope with chronic pain: a study of psychological and social factors

This reply slip lets the researchers know that you are interested in the study and are happy for them to have your contact details.

Please choose one of the options below

Young person:

I would like the researchers to contact me with more information about the study. ☐

or

I have enough information and would like to receive the study materials (consent form and questionnaire) from the researchers in the post. ☐

Parent:

I would like the researchers to contact me with more information about the study. ☐

or

I have enough information and would like to receive the study materials (consent form and questionnaire) from the researchers in the post. ☐

Young person's name and surname: _____

Parent's name and surname: _____

Postal Address:_____

_____

Post code: _____

Mobile/home phone number: _____

Email address:_____

Young person's Age: _____

Your GP will be informed about your participation to this study when we receive your questionnaire and consent form. Please write down your GP's details so we can contact them.

Young Person's GP surgery: _____

GP's name and surname:_____

Postal Address:_____

_____

Young person's signature: _____

Parent's signature:_____

Appendix E: Consent forms

SECTION OF CLINICAL & HEALTH PSYCHOLOGY
School of Health in Social Science
Medical School
Teviot Place
Edinburgh EH8 9AG
Tel: 0131-651 3972
Fax: 0131-651-3971

Young Person Consent Form (aged 12-15)

Project Title: How young people cope with chronic pain: a study of psychological and social factors

Please INITIAL (DO NOT TICK) the box if you agree:

1. I have read and understood the Participant Information Sheet for this study dated 18th August 2016 (version 5). I have had the opportunity to think about the information, ask questions and have had these clearly answered. ☐

2. I understand that taking part is entirely up to me and that I am free to change my mind and withdraw at any time, without giving any reason. This will not affect the care that I receive in any way. ☐

3. I understand that my personal details will not be shown to or shared with unauthorized people. ☐

4. I understand that my anonymized answers will be used by the researchers in scientific articles or presented at conferences, and may be used by researchers in the future. ☐

5. I understand that my clinical team will know that I'm taking part in the study and will provide information about my health condition to the research team. ☐

6. I understand that my GP will be informed about my participation in this study. ☐

7. I understand that data collected during the study may be looked at by people from the Sponsor (University of Edinburgh and NHS Lothian), from the NHS organisation or other authorities, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my answers. ☐

I agree to take part in the study. ☐

_____	_____	_____
Your Name	Date	Your signature
_____	_____	_____
Researcher	Date	Signature

SECTION OF CLINICAL & HEALTH PSYCHOLOGY
School of Health in Social Science
Medical School
Teviot Place
Edinburgh EH8 9AG
Tel: 0131-651 3972
Fax: 0131-651-3971

Young Person Consent Form (aged 16-18)

Project Title: How young people cope with chronic pain: a study of psychological and social factors

Please INITIAL (DO NOT TICK) the box if you agree:

1. I have read and understood the Participant Information Sheet for this study dated 18th August 2016 (version 5). I have had the opportunity to consider about the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that taking part is entirely up to me and that I am free to change my mind and withdraw at any time, without giving any reason. This will not affect the care that I receive in any way. ☐

3. I understand that my personal details will not be shown to or shared with unauthorized people. ☐

4. I understand that my anonymized answers will be used by the researchers in scientific articles or presented at conferences, and may be used by researchers in the future. ☐

5. I understand that my clinical team will know that I'm taking part in the study and will provide information about my health condition to the research team. ☐

6. I understand that my GP will be informed about my participation in this study. ☐

7. I understand that data collected during the study may be looked at by individuals from the Sponsor (University of Edinburgh and NHS Lothian), from the NHS organisation or other authorities, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my answers. ☐

   I agree to take part in the study. ☐

_____	_____	_____
Your Name	Date	Your signature
_____	_____	_____
Researcher	Date	Signature

Appendix F: Ethical approval

Lothian NHS Board

South East Scotland Research Ethics Committee 01

Waverley Gate
2-4 Waterloo Place
Edinburgh
EH1 3EG
Telephone 0131 536 9000

www.nhslothian.scot.nhs.uk

NHS Lothian

22 March 2016

Dr Nuno Ferreira
School of Health in Social Science
Teviot Place
Edinburgh
EH89AG

Date 22 March 2016
Your Ref
Our Ref

Enquiries to: [redacted]
Extension: [redacted]
Direct Line: [redacted]
Email: [redacted]

Dear Dr Ferreira

Study title: **Psychosocial predictors of paediatric chronic pain**
REC reference: **16/SS/0060**
IRAS project ID: **191155**

Thank you for your letter of 14 March 2016, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager, [redacted]

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).
Guidance on applying for NHS permission for research is available in the Integrated Research Application System, www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the

information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact [redacted] the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering letter on headed paper [Cover letter for study_paediatric chronic pain]	v2	14 March 2016
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Employers' Liability Insurance]		01 August 2015
GP/consultant information sheets or letters [contact letter to GPs]	v1	14 March 2016
Letter from funder [Wellcome Trust Award letter]		21 May 2015
Other [full policy_University Insurance]		13 July 2015
Other [University of Edinburgh_Clinical Trial Liability Insurance]		28 July 2015
Other [Professional Indemnity Insurance]		28 July 2015
Other [Request contact details]	v1	02 February 2016
Participant consent form [Parent consent form]	v2	14 March 2016
Participant consent form [Young person (10-15) consent form]	v2	14 March 2016
Participant consent form [Young person (16-18) consent form]	v2	14 March 2016

Participant information sheet (PIS) [Parent PIS]	v2	14 March 2016
Participant information sheet (PIS) [Young Person (10-15) PIS]	V2	14 March 2016
Participant information sheet (PIS) [Young Person (16-18) PIS]	v2	14 March 2016
REC Application Form [REC_Form_05022016]		05 February 2016
Research protocol or project proposal [Research proposal_Paediatric chronic pain]	v2	14 March 2016
Summary CV for Chief Investigator (CI) [N Ferreira Short CV 2016]	v1	02 February 2016
Summary CV for student [Leona Mc Garrigle CV 2016]	v1	02 February 2016
Validated questionnaire [Child battery]		02 February 2016
Validated questionnaire [added child test_8-12 y/o]		02 February 2016
Validated questionnaire [added child test 13-18 y/o]		02 February 2016
Validated questionnaire [Adult battery]		02 February 2016

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

NHS
Lothian

16/SS/0060	Please quote this number on all correspondence

With the Committee's best wishes for the success of this project.

Yours sincerely

[redacted]
Chair

Email [redacted]

Enclosures: "After ethical review – guidance for researchers"

Copy to: [redacted]

Appendix G: Research and Development Approval

Administrator: [redacted]
Telephone Number: 0141 232 1815
E-Mail: [redacted]
Website: www.nhsggc.org.uk/r&d

R&D Management Office
West Glasgow ACH
Dalnair Street
Glasgow G3 8SW

14 April 2016

Dr Leyla de Amicis
Research Assistant
University of Edinburgh
School of Health in Social Sciences
18 Buccleuch Place
Edinburgh EH8 9LN

NHS GG&C Board Approval

Dear Dr De Amicis,

Study Title:	**Psychosocial predictors of paediatric chronic pain**
Principal Investigator:	**Dr Leyla De Amicis**
GG&C HB site	**Royal Hospital for Children**
Sponsor	**NHS Lothian & the University of Edinburgh**
R&D reference:	**GN16MH115P**
REC reference:	**16/SS/0060**
Protocol no:	**V2; 14/03/16**

I am pleased to confirm that Greater Glasgow & Clyde Health Board is now able to grant **Approval** for the above study.

Conditions of Approval

1. **For Clinical Trials** as defined by the Medicines for Human Use Clinical Trial Regulations, 2004

    a. During the life span of the study GGHB requires the following information relating to this site
        i. Notification of any potential serious breaches.
        ii. Notification of any regulatory inspections.

It is your responsibility to ensure that all staff involved in the study at this site have the appropriate GCP training according to the GGHB GCP policy (www.nhsggc.org.uk/content/default.asp?page=s1411), evidence of such training to be filed in the site file.

2. **For all studies** the following information is required during their lifespan.
   a. Recruitment Numbers on a monthly basis
   b. Any change of staff named on the original SSI form
   c. Any amendments – Substantial or Non Substantial
   d. Notification of Trial/study end including final recruitment figures
   e. Final Report & Copies of Publications/Abstracts

Please add this approval to your study file as this letter may be subject to audit and monitoring.

Your personal information will be held on a secure national web-based NHS database.

I wish you every success with this research study

Yours sincerely,

[redacted]

Mrs [redacted]
Senior Research Administrator

Cc: [redacted]

University Hospitals Division

NHS Lothian

Queen's Medical Research Institute
47 Little France Crescent, Edinburgh, EH16 4TJ

FM/GM/Approval

6th April 2016

Research & Development
Room E1.12
Tel: 0131 242 3330

Email:
R&DOffice@nhslothian.scot.nhs.uk

Director: [redacted]

[redacted]
Paediatric Liasion Team
Child & Family Mental Health Services
3 Rillbank Terrace
Edinburgh
EH9 1LF

Dear [redacted]

Lothian R&D Project No: 2016/0109

Title of Research: Psychosocial predictors of paediatric chronic pain

REC No: 16/SS/0060

Participant Information Sheet:
(Parent) Version 2 Dated 14th March 2016
(Young Person 10-15) Version 2 Dated 14th March 2016
(Young Person 16-18) Version 2 Dated 14th March 2016

Consent Form:
(Parent) Version 2 Dated 14th March 2016
(Young Person 10-15) Version 2 Dated 14th March 2016
(Young Person 16-18) Version 2 Dated 14th March 2016

Protocol: Version 2 Dated 14th March 2016

I am pleased to inform you that this study has been approved for NHS Lothian and you may proceed with your research, subject to the conditions below. This letter provides Site Specific approval for NHS Lothian.

Please note that the NHS Lothian R&D Office must be informed if there are any changes to the study such as amendments to the protocol, recruitment, funding, personnel or resource input required of NHS Lothian.

Substantial amendments to the protocol will require approval from the ethics committee which approved your study and the MHRA where applicable.

Please inform this office when recruitment has closed and when the study has been completed.

I wish you every success with your study.

Yours sincerely

[redacted]
Deputy R&D Director

cc: [redacted]

Research and Development Support Unit
Ground Floor
Dumfries and Galloway Royal Infirmary
Bankend Road
Dumfries
DG1 4AP

NHS
Dumfries
& Galloway

Dr Nuno Ferreira
Lecturer in Clinical Psychology
The University of Edinburgh, Old Medical School, Doorway 6
Teviot Place
Edinburgh
EH8 9AG

Date: **19th April 2016**
Our ref: **16/DGY/013**
Study title: **Psychological Predictors of Paediatric Chronic Pain**
Protocol version approved: **Version 2 14/03/2016**
Amendments included: **N/A**

Dear Dr Nuno

Thank you for sending me details of your study with a request for management approval. I can confirm that the study review team has reviewed the documentation and on this basis I am pleased to inform you that your study has management approval for commencement within NHS Dumfries and Galloway.

It is a condition of this approval that everyone involved in this study abides by the guidelines/protocols laid down by this Health Board in respect of confidentiality and Research Governance. It is your responsibility to ensure you are familiar with these; please do not hesitate to seek advice if you are unsure.

We also note that it is the sponsor's responsibility to ensure that appropriate training is in place for all local investigators. It is important that all research must be carried out in compliance with the Research Governance Framework for Health and Community Care and the new EU Clinical Trials Directive (for clinical trials involving investigational medicinal products).

As part of the Health Board's responsibilities under Research Governance we will be monitoring studies at least on an annual basis. It is therefore important that all records in connection with the study are kept up to date and available for review. We are also required to inform you that details of your study will be entered onto our R&D database. As custodian of the information collated during this research project, you are responsible for ensuring the security of all personal information collected, in line with NHS Scotland IT Security Policies, until the destruction of this data.

If your study is adopted by UKCRN into a portfolio then please advise this department of recruitment figures by adding accrual data to that database on a monthly basis.

Research and Development Support Unit
Ground Floor
Dumfries and Galloway Royal Infirmary
Bankend Road
Dumfries
DG1 4AP

NHS
Dumfries
& Galloway

Please notify the R&D office immediately you become aware of any serious adverse events associated with this research.

You must contact the R&D Department if/when the project is subject to any minor or substantial amendments so that these can be appropriately assessed, and approved, where necessary. I understand that performance of this study will not infringe on NHS Dumfries and Galloway's ability to deliver our usual level of service.

May I take this opportunity to wish you every success with your project. Please do not hesitate to seek help and advice from the R&D Support Unit (ext 33164 and 33165) if there is anything which you feel you would like assistance with. I look forward to hearing about your work as it progresses and would appreciate a note of monthly recruitment figures, a short annual report and a final report when the study is complete.

Yours Sincerely

[redacted]
Research lead

Cc
SREDA database, [redacted]

PS Please contact R&D to arrange necessary Letter of Access for Dr Leyla De Amicis

Copies of Research Governance Framework document available via the website www.sehd.scot.nhs.uk/cso and then use the publications link.

NHS Forth Valley

Date: 20 Sept 2016
Your Ref:
Our Ref:
Direct Line: 01324 677564
Email: FV-UHB.RandD-depart@nhs.net
R&D ref: FV954

Dr Nuno Ferreira
School of Health in Social Science
Teviot Place
Edinburgh
EH8 9AG

Dear Dr Ferreira,

Study title: Psychosocial predictors of paediatric chronic pain
REC reference: 16/SS/0060

Following the favourable opinion from the South East Scotland Research Ethics Committee 01 on 22 March 2016, I am pleased to confirm that I formally gave Management Approval to the study above on 20 Sept 2016.

This approval is granted subject to your compliance with the following:

1. Any amendments to the protocol or research team must have Ethics Committee and R&D approval (as well as approval from any other relevant regulatory organisation) before they can be implemented. Please ensure that the R&D Office and (where appropriate) NRS are informed of any amendments as soon as you become aware of them.

2. You and any local Principal Investigator are responsible for ensuring that all members of the research team have the appropriate experience and training, including GCP training if required.

3. All those involved in the project will be required to work within accepted guidelines of health and safety and data protection principles, any other relevant statutory legislation, the Research Governance Framework for Health and Community Care and IHC-GCP guidelines. A copy of the Framework can be accessed via the Chief Scientist Office website at: http://www.cso.scot.nhs.uk/Publications/ResGov/Framework/RGFEdTwo.pdf
and ICH-GCP guidelines may be found at http://www.ich.org/LOB/media/MEDIA482.pdf

4. As custodian of the information collected during this project you are responsible for ensuring the security of all personal information collected in line with NHS Scotland IT security policies, until the destruction of this data.

5. You or the local Principal Investigator will be required to provide the following reports and information during the course of your study:

- A progress report **annually**
- Recruitment numbers on a **monthly** basis (if your study should be added to the NIHR research Portfolio you will receive a separate letter from the R&D Office detailing the steps to be taken)

- Report on SAEs and SUSARs if your study is a Clinical Trial of an Investigational Medicinal Product
- Any information required for the purpose of internal or external audit and monitoring
- Copies of any external monitoring reports
- Notification of the end of recruitment and the end of the study
- A copy of the final report, when available.
- Copies of or full citations for any publications or abstracts

The appropriate forms will be provided to you by the Research and Development office when they are needed. Other information may be required from time to time.

Yours sincerely

[redacted]

Pp
M
Medical Director

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Appendix Table A.1: Skewness and kurtosis z-scores for study variables

Measure	Skewness z-score	Kurtosis z-score
VAS	-2.44*	-1.61
CPAQ-A	-0.73	-0.66
PCS-C	0.72	-1.91
TSK-11	0.20	-1.49
FDI	2.00*	-1.72
BAPQ – Depression	2.05*	-0.09
BAPQ - Anxiety	2.30*	-0.44
PedsQL	-1.14	-1.55

*Values significantly different from a normal distribution when $p < .05$

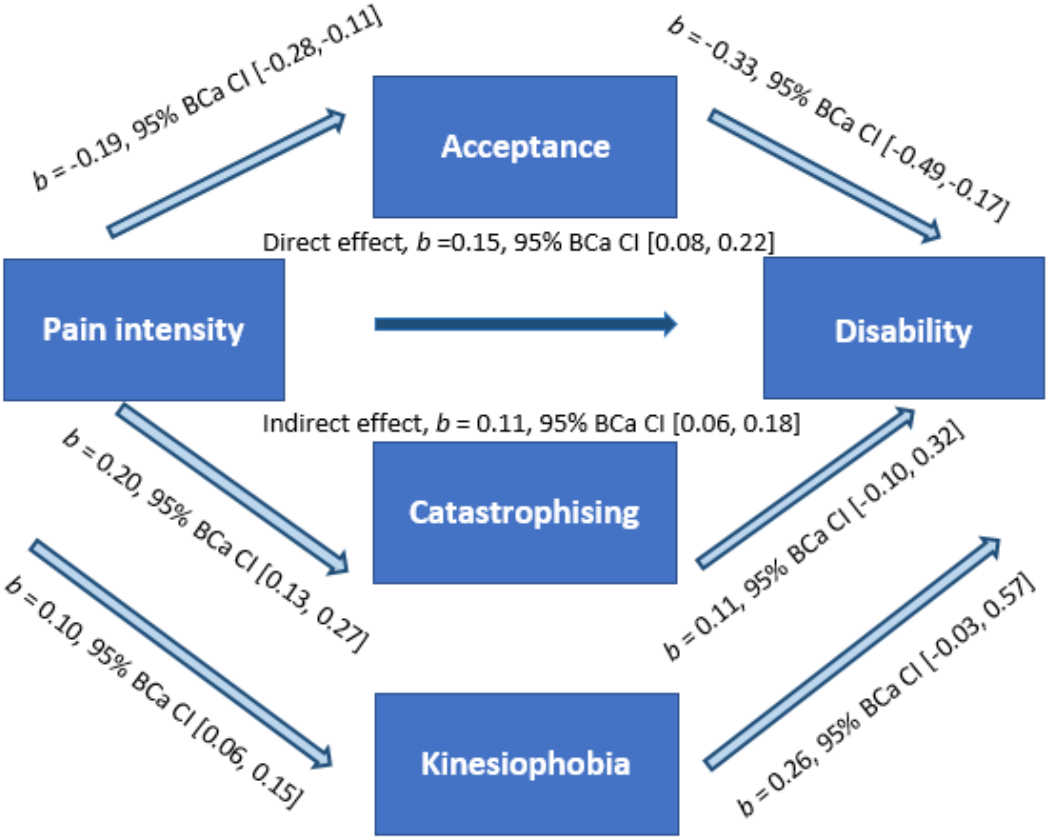
Appendix Table A.2: Simple mediation analyses for chronic pain adjustment

	Beta	Standard Error	95% BCa CI	
			Lower	Upper
Disability				
Total effect	0.27	0.04	0.19	0.34
Direct effect	0.18	0.03	0.11	0.25
Indirect effect (Acceptance)	0.09	0.02	0.05	0.14
Direct effect	0.17	0.04	0.10	0.25
Indirect effect (Catastrophising)	0.09	0.02	0.05	0.15
Direct effect	0.20	0.04	0.12	0.27
Indirect effect (Kinesiophobia)	0.07	0.02	0.04	0.12
Anxiety				
Total effect	0.09	0.02	0.06	0.12
Direct effect	0.07	0.02	0.03	0.10
Indirect effect (Acceptance)	0.02	0.01	0.01	0.04
Direct effect	0.05	0.02	0.01	0.08
Indirect effect (Catastrophising)	0.04	0.01	0.02	0.07
Direct effect	0.07	0.02	0.03	0.10
Indirect effect (Kinesiophobia)	0.02	0.01	0.01	0.05

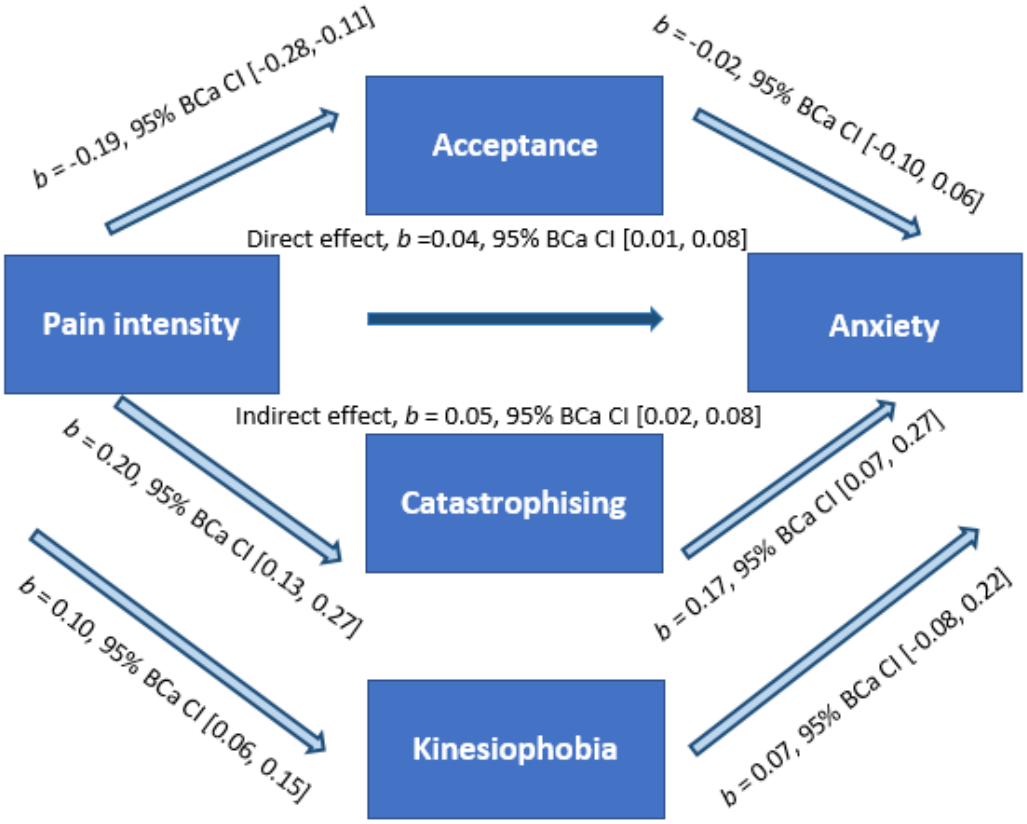
	Beta	Standard Error	95% BCa CI	
			Lower	Upper
Depression				
Total effect	0.10	0.02	0.07	0.13
Direct effect	0.07	0.15	0.04	0.10
Indirect effect (Acceptance)	0.03	0.01	0.01	0.05
Direct effect	0.06	0.02	0.03	0.08
Indirect effect (Catastrophising)	0.04	0.01	0.02	0.07
Direct effect	0.08	0.02	0.05	0.11
Indirect effect (Kinesiophobia)	0.02	0.01	0.01	0.04
Quality of Life				
Total effect	-0.42	0.06	-0.53	-0.31
Direct effect	-0.28	0.05	-0.38	-0.18
Indirect effect (Acceptance)	-0.14	0.04	-0.38	-0.18
Direct effect	-0.25	0.06	-0.36	-0.14
Indirect effect (Catastrophising)	-0.17	0.04	-0.26	-0.10
Direct effect	-0.27	0.05	-0.38	-0.17
Indirect effect (Kinesiophobia)	-0.15	0.04	-0.24	-0.08

BCa, Bias Corrected and accelerated; CI, confidence interval
5000 bootstrap samples

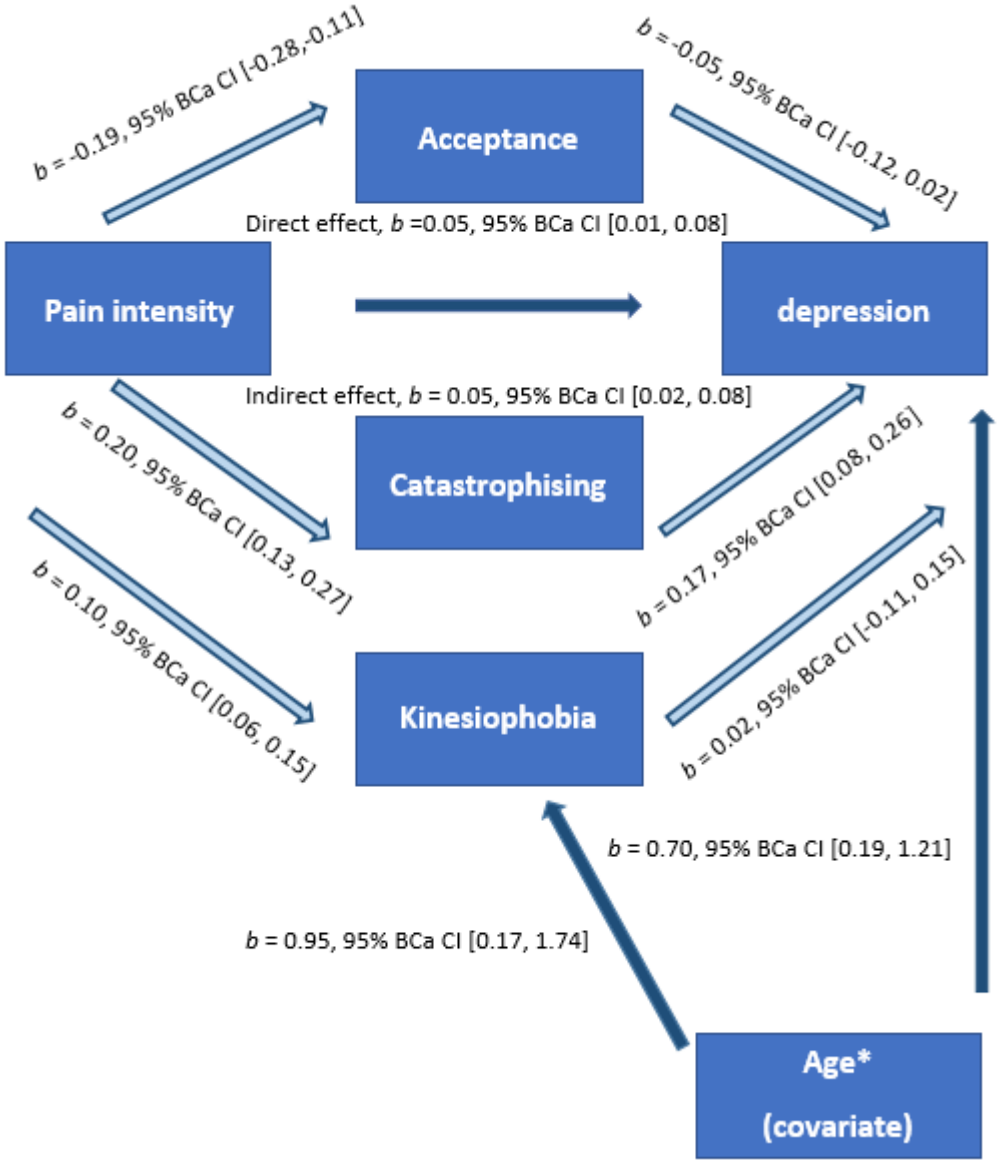
Appendix Fig. A.1: Multiple mediation model for disability



Appendix Fig A.2: Multiple mediation model for anxiety

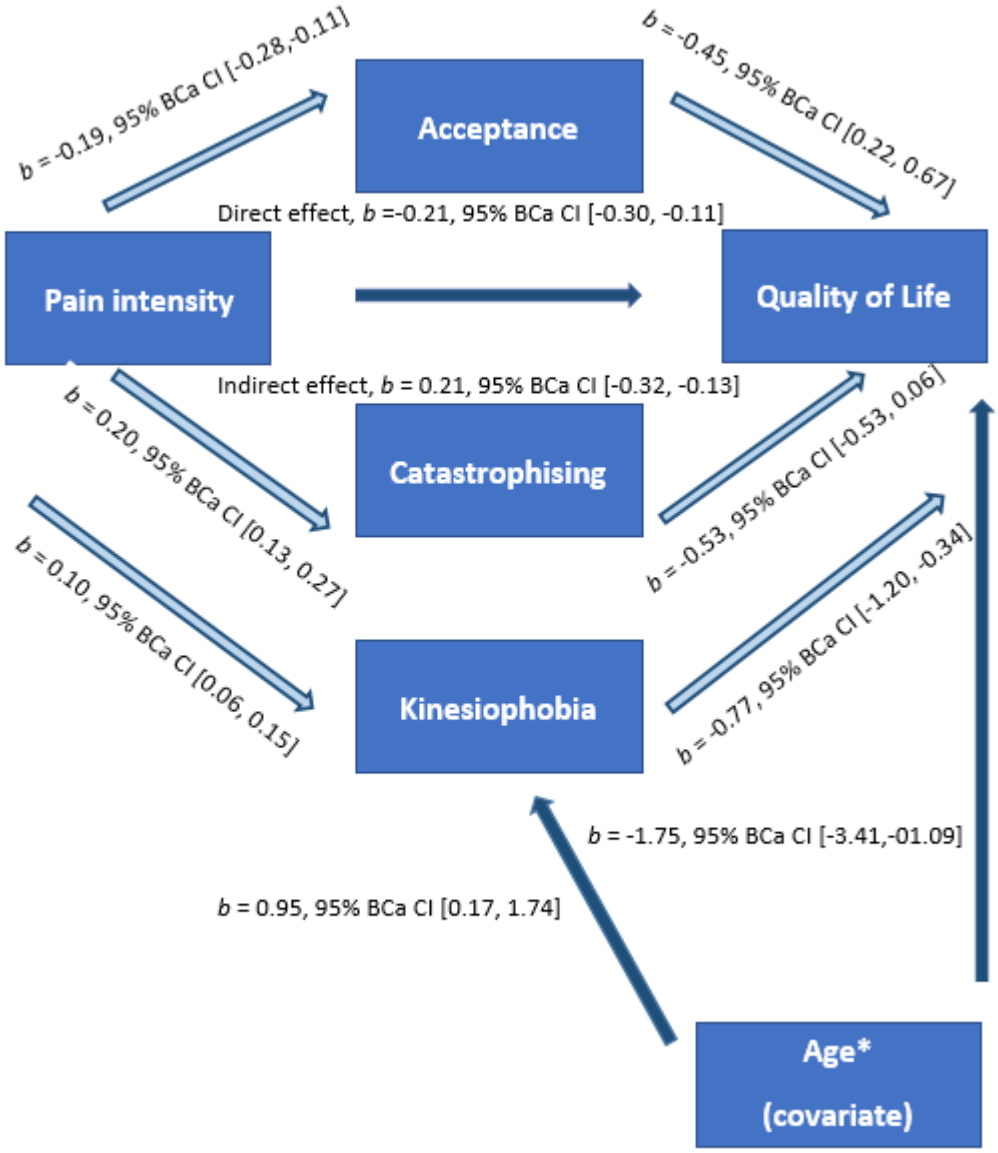


Appendix Fig A.3: Multiple mediation model for depression



***Age was not a significant predictor of acceptance or catastrophising**

Appendix Fig A.4: Multiple mediation model for quality of life



***Age was not a significant predictor of acceptance or catastrophising**

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